

ETS  
ISSUE BINDER

ETS AND  
RESPIRATORY  
DISEASES & CONDITIONS  
IN NON-SMOKING  
ADULTS & CHILDREN

III

2023379486

Clardy v. The Upjohn Co.

TRIAL NOTEBOOK

2023379487

**ETS AND  
RESPIRATORY DISEASES AND CONDITIONS  
IN NONSMOKING ADULTS AND CHILDREN**

**VOLUME III**

**2023379488**

THIS ISSUE BINDER IS INTENDED TO PROVIDE A BASIC,  
COMPREHENSIVE REVIEW OF THE SCIENTIFIC LITERATURE  
REGARDING A SPECIFIC TOPIC ON ETS AND THE HEALTH OF  
NONSMOKERS.

PRIMARY STUDIES AND REVIEWS HAVE BEEN HIGHLIGHTED  
TO IDENTIFY (1) USEFUL OR HELPFUL INFORMATION (YELLOW  
HIGHLIGHT) AND (2) ADVERSE RESULTS OR OPINIONS (BLUE  
HIGHLIGHT).

2023375189



**TABLE OF  
CONTENTS**

**2023379490**

**INTRODUCTION**  
**ETS AND CHILDHOOD AND ADULT RESPIRATORY DISEASE/SYMPTOMS**

This issue binder is designed to provide a comprehensive review of the major literature on environmental tobacco smoke and childhood and adult respiratory disease/symptoms. The book has been divided into subsections: (A) childhood respiratory disease/symptoms; (B) childhood pulmonary function; (C) compromised children such as asthmatics and children with cystic fibrosis; (D) otitis media; (E) adult respiratory disease/symptoms; (F) adult pulmonary function; (G) compromised adults; and (H) confounders.

Each section provides a short introduction to the topic. Major studies are preceded by a short abstract and followed by published critiques of the study. Each of the studies is highlighted to facilitate understanding of the issue: 1) favorable points are highlighted in yellow, and 2) unfavorable points are highlighted in blue. Tables and charts in the notebook are also highlighted in yellow (favorable) and blue (unfavorable).

2023378491

## STUDY ABSTRACTS

In the majority of cases, the abstract or summary that precedes the individual study is the actual quoted abstract of the article's authors. However, some authors did not present an appropriate summary or abstract in their article. In those cases, a brief summary of the article was prepared. The abstracts and summaries prepared by the individual authors of the studies are designated as "abstracts" and "summaries."

2023379492

## TABLE OF CONTENTS

INTRODUCTION AND TABLE OF CONTENTS.....TABLE OF CONTENTS

PARENTAL SMOKING AND CHILDHOOD RESPIRATORY HEALTH..TAB A	
MAJOR STUDIES.....	A1-A39
CAMERON ET AL., 1973.....	A1
HARLAP ET AL., 1974.....	A2
COLLEY, 1974.....	A3
COLLEY ET AL., 1974.....	A4
LEBOWITZ ET AL., 1976.....	A5
LEEDER ET AL., 1976.....	A6
BINDER ET AL., 1976.....	A7
KERREBIJN ET AL., 1977.....	A8
RANTAKALLIO, 1978.....	A9
SIMS ET AL., 1978.....	A10
FERGUSON ET AL., 1980.....	A11
FERGUSON ET AL., 1981.....	A12
BONHAM ET AL., 1981.....	A13
LOVE ET AL., 1981.....	A14
CAMACHO ET AL., 1982.....	A15
DODGE, 1982.....	A16
FERRIS ET AL., 1983.....	A17
SCHENKER ET AL., 1983.....	A18
EKWO ET AL., 1983.....	A19
GARDNER ET AL., 1984.....	A20
WARE ET AL., 1984.....	A21
FERGUSON ET AL., 1985.....	A22
PEDREIRA ET AL., 1985.....	A23
TOMINAGA ET AL., 1985.....	A24
WATKINS ET AL., 1986.....	A25
BURCHFIELD ET AL., 1986.....	A26
KERIGAN ET AL., 1986.....	A27
SALZMAN ET AL., 1987.....	A28
FLEMING ET AL., 1987.....	A29
COGSWELL ET AL., 1987.....	A30
TAYLOR ET AL., 1987.....	A31
OGSTON ET AL., 1987.....	A32
SOMERVILLE ET AL., 1988.....	A33
CHEN, 1989.....	A34
CORBO ET AL., 1989.....	A35
NEUSPIEL ET AL., 1989.....	A36
DOCKERY ET AL., 1989.....	A37
OWNBY ET AL., 1988.....	A38
MAJOR REVIEW: RUBIN & DAMUS, 1988.....	A39
PARENTAL SMOKING AND CHILDHOOD LUNG FUNCTION.....	B
MAJOR STUDIES.....	B1-B28
MANDI ET AL., 1974.....	B1
TAGER ET AL., 1976.....	B2
SCHILLING ET AL., 1977.....	B3

2023379493

YARNELL ET AL., 1979.....	B4
TAGER ET AL., 1979.....	B5
WEISS ET AL., 1980.....	B6
SPEIZER ET AL., 1980.....	B7
HASSELBLAD ET AL., 1981.....	B8
LEBOWITZ ET AL., 1982.....	B9
DODGE, 1982.....	B10
EKWO ET AL., 1983.....	B11
TAGER ET AL., 1983.....	B12
TASHKIN ET AL., 1984.....	B13
VEDAL ET AL., 1984.....	B14
LEBOWITZ ET AL., 1984.....	B15
SPINACI ET AL., 1985.....	B16
BERKEY ET AL., 1986.....	B17
TECULESCU ET AL., 1986.....	B18
CHEN ET AL., 1986.....	B19
BURCHFIEL ET AL., 1986.....	B20
LEBOWITZ ET AL., 1987.....	B21
LEBOWITZ ET AL., 1987.....	B22
O'CONNOR ET AL., 1987.....	B23
TSIMOYIANIS ET AL., 1987.....	B24
GOLD ET AL., 1989.....	B25
DOCKERY ET AL., 1989.....	B26
KAUFFMANN ET AL., 1989.....	B27
MAJOR REVIEW: WITORSCH & WITORSCH, 1989.....	B28
PARENTAL SMOKING AND COMPROMISED CHILDREN.....	C
MAJOR STUDIES.....	C1-C18
LEEDER ET AL., 1976.....	C1
GORTMAKER ET AL., 1982.....	C2
FERGUSON ET AL., 1985.....	C3
HORWOOD ET AL., 1985.....	C4
MURRAY ET AL., 1986.....	C5
ANDERSON ET AL., 1987.....	C6
EVANS ET AL., 1987.....	C7
TOYOSHIMA ET AL., 1987.....	C8
KERSHAW, 1987.....	C9
MURRAY ET AL., 1988.....	C10
SOMERVILLE ET AL., 1988.....	C11
STRACHAN, 1988.....	C12
OLDIGS ET AL., 1990.....	C13
SHERMAN ET AL., 1990.....	C14
WEITZMAN ET AL., 1990.....	C15
RUBIN, 1990.....	C16
GILLJAM ET AL., 1990.....	C17
YOUNG ET AL., 1991.....	C18
PARENTAL SMOKING AND OTITIS MEDIA IN CHILDREN.....	D
MAJOR STUDIES.....	D1-D13
SAID ET AL., 1978.....	D1
VINTHER ET AL., 1982.....	D2
KRAEMER ET AL., 1983.....	D3

2023379494

BLACK, 1985.....	D4
MOORHEAD, 1985.....	D5
PUKANDER ET AL., 1985.....	D6
FLEMING ET AL., 1987.....	D7
KALLAIL ET AL., 1987.....	D8
TAINIO ET AL., 1988.....	D9
STRACHAN ET AL., 1989.....	D10
ZIELHUIS ET AL., 1989.....	D11
* PUKANDER ET AL., 1990.....	D12
* STRACHAN, 1990.....	D13
ETS AND ADULT RESPIRATORY HEALTH.....	E
MAJOR STUDIES.....	E1-E4
LEE ET AL., 1986.....	E1
KOO ET AL., 1988.....	E2
* HOLE ET AL., 1989.....	E3
KOO ET AL., 1990.....	E4
ETS AND ADULT LUNG FUNCTION.....	F
MAJOR STUDIES.....	F1-F11
BOUHUYS ET AL., 1978.....	F1
* SHEPHARD ET AL., 1979.....	F2
* WHITE ET AL., 1980.....	F3
* COMSTOCK ET AL., 1981.....	F4
* KAUFFMANN ET AL., 1983.....	F5
JONES ET AL., 1983.....	F6
KENTNER ET AL., 1984.....	F7
LEBOWITZ ET AL., 1985.....	F8
HOSEIN ET AL., 1986.....	F9
* MASI ET AL., 1988.....	F10
* KALANDIDI ET AL., 1990.....	F11
ETS AND COMPROMISED ADULTS.....	G
MAJOR STUDIES.....	G1-G9
* STAHL ET AL., 1978.....	G1
SHEPHARD ET AL., 1979.....	G2
* DAHMS ET AL., 1981.....	G3
* ING ET AL., 1983.....	G4
* ROMER ET AL., 1983.....	G5
* KNIGHT ET AL., 1985.....	G6
WIEDEMANN ET AL., 1986.....	G7
* STANKUS ET AL., 1988.....	G8
BAILEY ET AL., 1990.....	G9
CONFOUNDERS.....	H
MAJOR STUDIES.....	H1-H30
* COLLEY, 1974.....	H1
* COLLEY ET AL., 1974.....	H2
HOLMA ET AL., 1977.....	H3
MELIA ET AL., 1977.....	H4
MELIA ET AL., 1979.....	H5
SPEIZER ET AL., 1980.....	H6

2023379495

LEBOWITZ ET AL., 1982.....	H7
NATIONAL INSTITUTES OF HEALTH, 1983.....	H8
EKWO ET AL., 1983.....	H9
LEBOWITZ ET AL., 1984.....	H10
BERWICK ET AL., 1984.....	H11
GARDNER ET AL., 1984.....	H12
HARRINGTON ET AL., 1985.....	H13
WATKINS ET AL., 1986.....	H14
KERIGAN ET AL., 1986.....	H15
STRACHAN ET AL., 1986.....	H16
ANDERSON ET AL., 1987.....	H17
• FLEMING ET AL., 1987.....	H18
MARTIN ET AL., 1987.....	H19
KOO ET AL., 1988.....	H20
MELIA ET AL., 1988.....	H21
GOREN ET AL., 1988.....	H22
NORDVALL ET AL., 1988.....	H23
MITCHELL ET AL., 1989.....	H24
POPE, 1989.....	H25
OSBORNE ET AL., 1989.....	H26
PLATT ET AL., 1989.....	H27
BRUNEKREEF ET AL., 1989.....	H28
BERWICK ET AL., 1989.....	H29
HURWITZ ET AL., 1991.....	H30

2023379496

G

2023379497



**ETS AND COMPROMISED ADULTS**

**2023379498**

### COMPROMISED ADULTS

The literature on environmental tobacco smoke includes a body of research on asthmatic adults. Studies have been conducted in order to attempt to determine whether there is a relationship between passive exposure to ETS and the development of asthma or the exacerbation of existing asthma in adults. The studies are varied in their results, and accordingly, no definitive conclusions have been reached by investigators. Following are the studies that examine ETS and its possible relation to asthma in adults.

2023379199

COMMENTS ON SELECTED STUDIES: ETS AND COMPROMISED ADULTS

Stahle, et al., 1978

The authors suggest that tobacco smoke exposure might trigger asthma attacks by means of an allergic reaction.

Shephard, et al., 1979

Reported that asthmatic subjects did not appear to have an unusual sensitivity to tobacco smoke exposure.

Dahms, et al., 1981

Five of the ten subjects specifically reported sensitivity to tobacco smoke before their inclusion in this study.

Ing, et al., 1983

This study investigated only six subjects.

Romer, et al., 1983

The authors concede that the small subject population of this study indicates that the results must be taken with caution.

Knight, et al., 1985

Only six subjects were studied.

Wiedemann, et al., 1986

The authors report that passive smoking presents no acute respiratory risk to young asymptomatic asthmatic patients.

Stankus, et al., 1988

Only 21 subjects were included and all had complained of respiratory symptoms upon previous exposure to environmental tobacco smoke.

Bailey, et al., 1990

No relationship was observed between passive smoking and pulmonary function of asthmatic subjects.

2023379500

**2023379501**

Stahle, I., Tibbling, L. "TOBACCO ALLERGY IN PATIENTS WITH BRONCHIAL ASTHMA" Lakartidningen 75(17): 1711-1713, 1978.

ABSTRACT. In 21 per cent of 233 patients with exogenous asthma bronchiale asthma attacks were triggered by inhalation of tobacco extract. A positive intracutaneous test with tobacco extract was far more common ( $p < 10^{-6}$ ) in patients with a positive than those with a negative response to provocation by tobacco extract. After three years of hyposensitization 84 per cent showed a negative response to provocation. The conclusion is that tobacco smoke may trigger asthma by means of an allergic reaction. Exposure to tobacco smoke must be investigated on the basis of case reports on asthmatics. Asthmatics who are hypersensitive to tobacco smoke should be afforded a smoke-free work and leisure environment.

2023379502

## TOBACCO ALLERGY IN PATIENTS WITH BRONCHIAL ASTHMA

by

I. Stahle and L. Tibbling

In 21 per cent of 233 patients with exogenous asthma bronchiale asthma attacks were triggered by inhalation of tobacco extract. A positive intracutaneous test with tobacco extract was far more common ( $p < 10^{-4}$ ) in patients with a positive than those with a negative response to provocation by tobacco extract. After three years of hypo-sensitization 84 per cent showed a negative response to provocation. The conclusion is that tobacco smoke may trigger asthma by means of an allergic reaction. Exposure to tobacco smoke must be investigated on the basis of case reports on asthmatics. Asthmatics who are hypersensitive to tobacco smoke should be afforded a smoke-free work and leisure environment.

Bronchial asthma is a diagnosis based on the symptomatology. From the standpoint of treatment and prognosis, the disease is usually classified into an exogenous and an endogenous form, between which, however, one finds floating transitions.

The exogenous form is triggered by a specific allergen and is most common among children and youth.

The endogenous form, in which specific antigens cannot be demonstrated as the triggering factor, is primarily seen in persons over 35 years old. Patients with this form of asthma often display the picture of a chronic bronchitis between attacks, and their asthma complaints are exacerbated during periods of infection. In a study of the effect of tobacco smoke on asthmatics, it is therefore reasonable to assume that endogenous asthma is exacerbated if the patient is an active smoker, since tobacco smoking gives

2023379503

**NOTE: THIS IS NOT A  
CERTIFIED TRANSLATION**

**TOBACCO ALLERGY IN PATIENTS WITH BRONCHIAL ASTHMA  
[Tobaksallergi hos patienter med asthma bronchiale]**

**by**

**I. Stahle and L. Tibbling**

**of**

**Kolmarden Hospital, Kolmarden, Sweden**

**from**

***Läkartidningen* 75(17):1711-1713, 1978**

**Translation from Swedish**

**ANHD/pb**

**2023379504**

rise to a chronic bronchitis. For both the smoking and the nonsmoking asthmatics, however, it is of interest to know whether tobacco smoke, besides its nonspecific bronchitis stimulating effect, can give rise to asthma attacks on the basis of tobacco allergy.

#### *Purpose*

The purpose of this study was to investigate in a retrospective records study the incidence of asthma attacks after inhalation provocation with tobacco extract in patients with bronchial asthma and to put the results of the provocation tests into a relationship with the intracutaneous tests, smoking consumption, anamnestic complaints regarding tobacco smoke, and sensitivity to other antigenic substances. The intent was also to investigate retrospectively whether a three-year hyposensitization therapy with tobacco extract in nonsmokers would cause any change in provocation tests that were positive before the treatment.

#### *Material and Methods*

The retrospective study encompasses all patients who were referred during 1971 to the Kolmarden Hospital for an asthma examination and who, either after an intracutaneous test displayed positive reactions to some specific allergen, or who had a history which gave rise to suspicion of hypersensitivity to some specific substance. No pure cases of endogenous asthma were included.

The material included 125 men and 108 women, totalling 233. The age distribution and the average time for which the patients had had asthma at the time of examination are shown in Fig. 1.



In the study on the effect of hyposensitization with tobacco extracts, a sample was included which had been treated during the years 1969-71. It consisted of 31 patients (16 men and 15 women), all nonsmokers with positive provocation tests with tobacco extracts, with a history of tobacco hypersensitivity, and considered to be in need of a hyposensitization therapy. During a period of three years, these patients received monthly subcutaneous injections of a maximum of 1 ml of tobacco extract. After the hyposensitization therapy, provocation tests were conducted once more but no intracutaneous tests were performed except in a few isolated cases.

The tobacco extract used was manufactured by Vitrum upon special order by the Kolmarden Hospital. The extract was made from American tobacco by suspending the tobacco in a physiologic saline solution, i.e., by the same operating principle as used to make other allergens. This tobacco extract differs from the other Vitrum solutions used in this country for tobacco tests, the latter being made by allowing tobacco smoke to bubble through a saline solution.

For the intracutaneous test with tobacco extract, 0.1 ml of the extract diluted to 1 to 100 was used. A positive intracutaneous test was considered to be present with a spot size of more than 20 mm diameter. For the inhalation provocation, tobacco extract was used in a dilution of 1:10. If, after two inhalations, no bronchoconstriction occurred, the inhalation was repeated 5 minutes later with three inhalations and 15 minutes later with five inhalations. The provocation test was evaluated as positive if, following the test, sibilant rhonchi could be auscultated over both lung fields or if the average of three peak flow measurements declined by more

than 20% compared with measurements before the provocation. Suspicion of tobacco hypersensitivity was considered present if the patient, when giving his history, reported suffering aggravation of his asthma complaints upon his exposure to tobacco smoke. Such suspicion is called a "history of tobacco hypersensitivity" in the following.

The allergen extracts from dust, mold, pollen, animal epithelium, and food substances were all standard Vitrum solutions. At the time when the study was performed, neither RAST or PRIST was available.

Fischer's exact test was used for the statistical processing.

### *Results*

#### *Skin Test with Tobacco Extracts*

Of 233 asthma patients, 39 displayed a positive intracutaneous test (Table I). Of these, 21 were found among the 48 provocation-positive patients and 18 among the other 189 in the study sample. The frequency of positive skin tests among the provocation positives (42%) differs highly significantly from the frequency of positive skin tests among the provocation negatives (10%):  $p < 10^{-6}$ .

#### *Provocation with Tobacco Extracts*

Out of 233 patients, 48 had a positive provocation test with tobacco extract, i.e., 21% (see Fig. 1 and Table I). No difference existed between the sexes. The tobacco hypersensitivity was proportionally somewhat more common among the older patients. In ten of the 48 cases that were positive to tobacco extracts provocation, the tobacco extract was the only one of all the allergen extracts tested which induced asthma attacks, constituting almost 4% of the entire sample.

### *Anamnestic Tobacco Hypersensitivity*

In 79% (39/48) of the provocation-positive patients, the history indicated hypersensitivity to tobacco smoke. The corresponding figures for the provocation negatives were 11% (21/185), which differs significantly ( $p < 10^{-19}$ ) from the provocation positive.

### *Smoking Habits*

In the provocation-negative group of 185 patients, 38% of the men and 35% of the women were smokers, figures which do not differ from the national average. In the provocation-positive group, 27% (13/48) were smokers.

*Table 1. Outcome of intracutaneous test and inhalation provocation with different allergen extracts in 233 patients with bronchial asthma. Figures are given in per cent*

	To- bacco	Dust	Mold	Pollen	Animal epithe- lium	Food sub- stances
125 men:						
Positive intracutaneous test	15	20	5	54	51	40
Positive provocation test	24	9	3	46	21	14
108 women:						
Positive intracutaneous test	24	28	14	67	44	58
Positive provocation test	24	23	8	46	31	23

### *Other Allergens*

The result of the intracutaneous test and provocation with extracts from tobacco, dust, mold, pollen, animal epithelium, and food substances is shown in Table I. Almost half were pollen allergics (121/233), every fifth an animal allergic (52/233), and/or tobacco allergic (48/233) and every seventh one was allergic to dust (32/233).

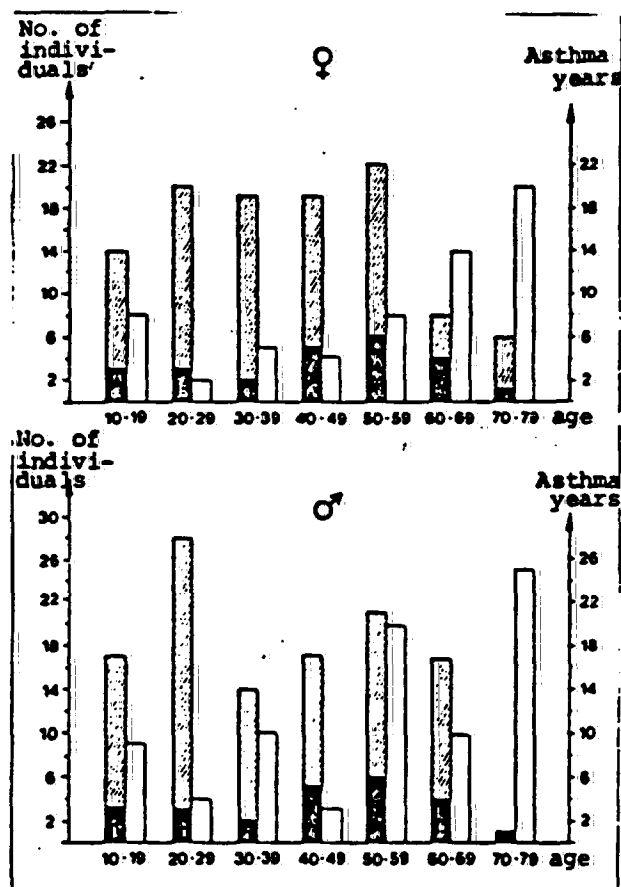


Fig. 1. Age distribution of 125 men and 108 women with bronchial asthma. The left-half of the column indicates the number of individuals within an age group, the black columns the number of cases displaying positive provocation test with tobacco extracts. The right blank half of the columns indicates the number of years for which the respective age groups had bronchial asthma on the average (asthma years).

The greatest discrepancy between positive intracutaneous test and provocation test was present for the food substance extract.

#### *Hyposensitization Therapy with Tobacco Extracts*

Of the 31 nonsmokers with positive provocation tests from tobacco extracts and who were sensitized during a three-year period, 13 (42%) had a positive intracutaneous test before the treatment. The provocation test with tobacco extract after the treatment period had ended was negative in 26 cases (84%).

In only five cases of the 13 skin positive cases before treatment, were new intracutaneous tests performed after the treatment. Four of them had negative results.

#### *Discussion*

Reactions of the airways during exposure to tobacco smoke have been the subject of numerous studies. Speer (1968) studied the subjectively reported complaints of 191 allergic and 250 nonallergic nonsmokers when they were exposed to tobacco smoke. Coughing was reported in 46% by allergics and in 25% of nonallergics, sneezing in 23 and 4% respectively, eye irritation in 67 and 29% respectively.

O'Connell and Logan (1974) studied the role of exposure to tobacco smoke in 400 asthmatic and 228 nonasthmatic children. If any of the parents smoked, the complaints of the asthmatic child were aggravated in 67% by exposure to smoke as opposed to 26% if neither parents smoked. This difference could be explained by the fact that the asthmatic children exposed to tobacco smoke daily have been sensitized to tobacco smoke. Zussman (1970) published the results of a hyposensitization therapy of 16

atopic persons, most of them with hayfever, who were clinically tobacco allergic. In ten of these, the symptoms decreased by more than 75%. In the remaining six cases, the symptoms were cut in half after the hyposensitization treatment. These results speak in favor of an allergen in tobacco smoke.

In 1976, Becker et al. isolated a glucoprotein with antigenic properties from both tobacco extract and tobacco smoke condensate, to which almost one-third of the smokers and nonsmokers reacted positively in intracutaneous tests.

#### *Tobacco Allergy?*

In this study, provocation with tobacco extract was used for the first time against the "shock organ", at which time every fifth asthmatic reacted with attacks of asthma. The highly significant difference in the frequency of positive skin tests between provocation-positive and provocation-negative asthmatics testifies that the tobacco smoke transports potentially allergenic substances.

The fact that 84% of the provocation-positive nonsmokers were provocation negative after hyposensitization further strengthens this belief. Possibly also speaking in favor of this is the observation that 73% of the provocation-positive patients were nonsmokers and therefore should have been sensitized through passive smoking. This latter agrees well with O'Connell's and Logan's (1974) finding that children with asthma who were exposed to tobacco smoke suffer more complaints if they come from smoking than if they come from smoke-free home environments.

### *Tobacco Smoke Versus Tobacco Extract*

The fact that one-third of the asthmatics who reported anamnestic aggravation of their asthma complaints in smoke-polluted environments did not have a positive provocation test may have many causes. The composition of the tobacco smoke and the tobacco extract are different in part. Many of the gases that are formed upon condensation or combustion during smoking have a nonspecific bronchus-irritating effect and are not found in the tobacco extract. Thus, for instance, the high content of nitrous gases in tobacco smoke may be suspected of triggering asthma attacks.

It is therefore possible that asthma attacks are more common among patients who are exposed to tobacco smoke than is indicated in this study with tobacco extract where several nonspecifically acting gases were eliminated. Of course, this does not exclude the possibility that the tobacco extract may, in part, have been able to trigger nonspecific asthmatic reactions in those who remained provocation positive. One possibility of solving this riddle will be obtained when the RAST test is available with reliable tobacco extracts.

### *Trigger Mechanism*

Except for an antigen-antibody reaction and nonspecific reactions, an additional trigger mechanism may also be suspected of having caused the asthma complaints in passive and active smokers, i.e., infection. Cameron et al. (1969) observed that acute upper respiratory infections were more common among children from homes with parents who smoked than among children with nonsmoking parents. Harlap and Davies (1974) studied the incidence of bronchitis and pneumonia in 10,000 newborn children in

relationship to cigarette consumption of the mother. The more the mother smoked, the greater the risk the newborn child ran of contracting a respiratory infection. Finklea et al. (1971) found that the antibody titers after a sustained infection were significantly lower in smokers than in nonsmokers.

The fact that in this study, 84% of the tobacco extract provocation-positive patients became provocation negative after hyposensitization therapy could perhaps be ascribed in part to a reduced infection susceptibility with a smaller tendency to react to any possible nonspecific irritation. An infection mechanism, however, could not explain the highly significant differences in the intracutaneous tests between provocation-positive and provocation-negative patients. It is also improbable that if nonspecific reactions consequent to bronchitis underlay a positive provocation test, the latter would have been influenced at such a high frequency by the general treatment during the three-year period when the hyposensitization therapy was underway, since the majority of the patients had been treated for their bronchial asthma for at least six years before the tests had begun.

The tobacco-promoting asthma attacks in smokers showed the tendency of smokers to continue tobacco smoking despite somatic complications, which is an illustration of the strength of the nicotine dependence (Martelius, Tibbling 1977).

In some cases, presumably, the patient is unaware of the relationship between his asthma and smoke consumption (Blue 1970).



*Smoke Polluted Air—a health hazard*

Behind the cause of the asthma attacks in both the active and the passive smoker, one probably finds not only allergic but nonspecific and infectious mechanisms. For the patient, the underlying cause should be of no interest unless a hyposensitization treatment is available to him. However, it appears appropriate in conformance with other allergy treatments, to eliminate, above all, the agent which gives rise to the complaint, i.e., tobacco smoke. For this, however, it will be necessary for the examining doctor to be aware that tobacco smoke can cause asthma attacks in at least every fifth asthmatic and that the majority of them are nonsmokers.

In those cases when smokers in the environment of the asthmatic cannot be persuaded to abstain from tobacco smoking, something which is unquestionably difficult, a hyposensitization treatment may be a conceivable alternative.

REFERENCES

- BECKER C G, DUBIN T, WIEDERMANN H  
P: Hypersensitivity to tobacco antigen. *Proc Natl Acad Sci USA* 73: 1712-1716 1976
- BLUE J A: Cigarette asthma and tobacco allergy. *Ann Allergy* 28: 110-115 1970
- CAMERON P, KOSTIN J S, ZAKS J M: The health of smokers' and nonsmokers' children. *J Allergy* 43: 336-341 1969
- FINKLEA J F, HASSELBLAD V, RIGGAN W B, NELSON W C, HAMMER D S, NEWILL V A: Cigarette smoking and hemagglutination inhibition response to influenza after natural disease and immunization. *Am Rev Resp Dis* 104: 368 1971
- HARLAP S, DAVIES A: Infant admissions to hospital and maternal smoking. *Lancet* ii: 529 1974
- HARTELIUS J, TIBBLING L: Nicotine dependence and smoking cessation programs: A review. *World Smoking Health* 2: 4-10 1977
- O'CONNELL E J, LOGAN G B: Parental smoking in childhood asthma. *Ann Allergy* 32: 142-145 1974
- SPEER F: Tobacco and the nonsmokers. *Arch Environ Health* 16: 443-446 1968
- ZUSSMAN B M: Tobacco sensitivity in the allergic patient. *Ann Allergy* 28: 371-377 1970

**2023373515**

Shephard, R.J., Collins, R., Silverman, F. "Passive" Exposure of Asthmatic Subjects to Cigarette Smoke" Environmental Research 20: 392-402, 1979.

SUMMARY: Fourteen asthmatic subjects volunteered for a controlled trial of 2-hr passive exposure to cigarette smoke. Seven cigarettes were burnt in a closed room of 14.6-m<sup>3</sup> capacity, producing a carbon monoxide concentration 24 ppm above ambient and a suspended particulate concentration of 2-4 mg\*m<sup>3</sup>. Most symptomatic responses were as in normal individuals, but there were more complaints of wheezing (36%) and tightness in the chest (43%). Changes of pulmonary function were slight. Relative to the corresponding control exposure, there was a small decrease of total lung capacity as assessed by helium mixing (P 0.02), possibly indicating an effect of the smoke on small airways. There was also some evidence of arousal and or emotional excitement, including a slight tachycardia (at 80-min exposure, P 0.05) and a slight increase of forced vital capacity (P 0.05 at 90-min exposure). However, dynamic lung volumes (FEV<sub>1.0</sub>, V<sub>max50%vc</sub>, V<sub>max25%vc</sub>) were unaltered. Examining separately the four subjects who claimed sensitivity to cigarette smoke, the only significant difference from the remaining asthmatic individuals was a greater FEV<sub>1.0</sub> relative to the corresponding time in the control exposure. Our data thus do not suggest that asthmatic subjects have an unusual sensitivity to cigarette smoke.

2023378516

## "Passive" Exposure of Asthmatic Subjects to Cigarette Smoke

ROY J. SHEPHARD, R. COLLINS, AND F. SILVERMAN

Department of Preventive Medicine and Biostatistics, University of Toronto and The Gage Research Institute, Toronto, Ontario M5S 1A1, Canada

Received March 4, 1979

Fourteen asthmatic subjects volunteered for a controlled trial of 2-hr passive exposure to cigarette smoke. Seven cigarettes were burnt in a closed room of 14.6-m<sup>3</sup> capacity, producing a carbon monoxide concentration 24 ppm above ambient and a suspended particulate concentration of 2-4 mg·m<sup>-3</sup>. Most symptomatic responses were as in normal individuals, but there were more complaints of wheezing (36%) and tightness in the chest (43%). Changes of pulmonary function were slight. Relative to the corresponding control exposure, there was a small decrease of total lung capacity as assessed by helium mixing ( $P < 0.02$ ), possibly indicating an effect of the smoke on small airways. There was also some evidence of arousal and/or emotional excitement, including a slight tachycardia (at 60-min exposure,  $P < 0.05$ ) and a slight increase of forced vital capacity ( $P < 0.05$  at 90-min exposure). However, dynamic lung volumes (FEV<sub>1</sub>,  $\dot{V}_{max}$ ,  $\dot{V}_{max}$ ,  $\dot{V}_{max}$ ) were unaltered. Examining separately the four subjects who claimed sensitivity to cigarette smoke, the only significant difference from the remaining asthmatic individuals was a greater FEV<sub>1</sub> relative to the corresponding time in the control exposure. Our data thus do not suggest that asthmatic subjects have an unusual sensitivity to cigarette smoke.

### INTRODUCTION

There is now good documentation concerning the accumulation of particulate matter, irritant gases, and vapors that results from the smoking of cigarettes in a closed and poorly ventilated space (see Sebben *et al.*, 1977; Pimm *et al.*, 1978; Shephard *et al.*, 1978). Nevertheless, physiological responses to such pollutants are remarkably slight in normal adults. The breakup of the tear film is significantly accelerated (Basu *et al.*, 1978), but both acute (Pimm *et al.*, 1978; Shephard *et al.*, 1979a) and chronic (Schilling *et al.*, 1977) changes of airway resistance are usually small and statistically insignificant even when high concentrations of smoke have been used and subjects have been required to perform intermittent exercise during exposure (Shephard *et al.*, 1979a).

Argument continues over the existence of respiratory allergies to tobacco smoke (Speer, 1968; Zussman, 1970; Blue, 1970; Savel, 1970). Although formal immune responses have yet to be demonstrated, wheezing following "passive" exposure to cigarettes is more than twice as frequent in asthmatics as in non-asthmatics (Shephard *et al.*, 1979b). It was thus thought of interest to make an assessment of symptoms and objective airway responses in a group of asthmatic adults passively exposed to controlled concentrations of cigarette smoke.

### METHODS

**Subjects and experimental plan.** The subjects were 14 volunteers attending the Asthma Clinic of The Gage Research Institute. Physical characteristics and baseline lung function data are given in Table 1. The diagnosis was reached ac-

TABLE 1  
PHYSICAL CHARACTERISTICS OF SUBJECTS (MEAN  $\pm$  SD, RANGE) AND BASELINE PULMONARY  
FUNCTION DATA (PERCENTAGE PREDICTED\*  $\pm$  SD)

Physical characteristic	Men (n = 9)	Women (n = 5)	All subjects (n = 14)
Age (years)	44 $\pm$ 14 (27-65)	33 $\pm$ 8 (19-38)	
Height (cm)	173.6 $\pm$ 10.0 (161-194)	163.6 $\pm$ 8.6 (157-178)	
Weight (kg)	73.7 $\pm$ 10.3 (54.3-86.1)	62.3 $\pm$ 7.7 (56.5-75.3)	
FVC	98 $\pm$ 19 (57-128)	107 $\pm$ 12 (91-123)	101 $\pm$ 17 (57-128)
FEV <sub>1.0</sub>	68 $\pm$ 19 (30-91)	84 $\pm$ 23 (60-113)	74 $\pm$ 21 (30-113)
$\dot{V}_{max, 25\%VC}$	44 $\pm$ 23 (16-81)	66 $\pm$ 39 (21-106)	52 $\pm$ 30 (16-106)
FRC	90 $\pm$ 11 (76-104)	100 $\pm$ 18 (83-125)	94 $\pm$ 14 (76-125)
RV	93 $\pm$ 27 (63-152)	98 $\pm$ 27 (67-136)	95 $\pm$ 26 (63-152)
TLC	99 $\pm$ 10 (87-118)	102 $\pm$ 10 (94-119)	100 $\pm$ 10 (87-119)

\* Based on norms adopted for Toronto laboratories by Toronto Interhospital Respiratory Disease Committee.

according to the standard criteria of The Gage Research Institute, namely: (i) a history consistent with diffuse intermittent airway obstruction, and (ii) diffuse expiratory bronchi and/or reversible airway obstruction demonstrated by a  $>15\%$  increase of FEV<sub>1.0</sub> or  $\dot{V}_{max, 25\%VC}$  20 min following inhalation of salbutamol. Associated chronic bronchitis or pulmonary emphysema was not a contraindication to participation but no tests were carried out during acute respiratory infections or exacerbations of the asthma. All subjects continued with their normal medication on experimental days (Table 2). The median methacholine sensitivity (as judged from the concentration needed to induce a 20% fall of FEV<sub>1.0</sub>) was 3.1 mg/ml, and the gain of  $\dot{V}_{max, 25\%VC}$  with four puffs of salbutamol ranged from 10 to 341% (median 30%).

Each subject sat in a small (14.6 m<sup>3</sup>) room for 2 hr on two occasions: at one visit, the room contained ambient air, and on the other occasion it was heavily contaminated by cigarette smoke from a smoking machine, the order of the experiments being determined by lot. A battery of lung function tests was performed before, during, and after exposure, and heart rates were also monitored at 10-min intervals. Subjects were questioned as to symptoms they anticipated on entering the chamber, and those they actually encountered on leaving the chamber.

**Smoke generation.** The cigarette smoking machine was of the type described by

2023375518

TABLE 2  
NORMAL MEDICATION, CONCENTRATION OF METHACHOLINE NEEDED TO INDUCE 20% FALL OF FEV<sub>1</sub>, AND CHANGE IN FUNCTION INDUCED BY FOUR PUFFS OF VENTOLIN

Subject	Medication						Methacholine sensitivity	Percentage change of function after four puffs of ventolin		
	"Fedral"	"Choladyl"	"Beclivent"	"Alupent"	"Prednisone"	"Ventolin"		FVC (%)	FEV <sub>1</sub> (%)	$\dot{V}_{max}$ (L/min)
Hr	R	—	—	—	—	P	Not done	Not done	Not done	Not done
Ba	—	R	—	—	—	P	>25 mg/ml	2	8	29
Ch	—	R	R	—	—	—	3.1	22	48	Not done
Co	—	—	—	—	—	O	1.6	Not done	Not done	Not done
Sp	—	—	R	—	—	P	12.3	3	22	Not done
Hr	—	—	R	—	R	P	1.6	30	53	99
Fe	—	R	R	—	—	—	1.6	9	48	59
Se	—	P	R	—	R	P	3.1	10	113	204
Ba	—	P	—	—	P	P	0.8	9	11	10
Mo	—	—	—	—	—	P	Not done	0	10	25
Hr	—	—	R	R	—	P	Not done	2	7	31
Lo	—	R	R	—	—	P	Not done	9	24	141
Ro	R	—	—	—	—	P	Not done	0	11	28
Mo	—	—	—	—	—	—	25 mg/ml	-3	1	19

\* Dimediholates as needed, R = regular, O = occasional, P = as needed. Fedral = theophylline + ephedrine + phenobarbital, prednisone = prednisolone sulphate, ventolin = salbutamol, choladyl = oxtriphylline, beclivent = beclomethasone, and alupent = delta cortisone.

2023378519

Wynder and Hoffman (1967). Prior to exposure, four cigarettes were "smoked" simultaneously, with combustion of one further cigarette at 30-min intervals in order to maintain smoke concentrations. A small peristaltic pump connected to a series capacity vessel drew one brisk (2-sec) but controlled (35-ml) puff through the apparatus, discharging the "mainstream" smoke into the room after passage through the solenoids, capacity vessel, and pump. "Sidestream" smoke escaped directly into the room.

The cigarettes used were a popular 85-mg filter type, with reported values for tar and nicotine content of 19 and 14 mg, respectively; they were smoked to a butt length of about 23 mm. Preliminary experiments established that with the pattern of combustion used, a carbon monoxide concentration of 24 ppm above ambient was developed and sustained. The initial suspended particulate concentration was  $>4 \text{ mg/m}^3$ , but values dropped to  $\sim 2 \text{ mg/m}^3$  over the 2-hr exposure period.

*Pulmonary function studies.* At the beginning and the end of each 2-hr experiment the relaxed vital capacity (RVC), functional residual capacity (FRC), residual volume (RV), and total lung capacity (TLC) were measured by a closed-circuit helium katharometer System (Collins modular lung analyzer).

Flow/volume loops were measured on entering the exposure chamber, and at

TABLE 3  
POTENTIAL SYMPTOMS DURING "PASSIVE" CIGARETTE EXPOSURE—NUMBER OF SUBJECTS ANTICIPATING EACH SYMPTOM, AND REPORTED SEVERITY ON SIX-POINT SCALE WHEN COMPLETING A QUESTIONNAIRE AT THE END OF EXPOSURE

Symptom	Number anticipating symptom (n = 13) <sup>a</sup>	Severity (n = 14)					
		Absent (0)	Trace (1)	Mild (2)	Moderate (3)	Severe (4)	Incapacitating (5)
Nasal discharge or stuffiness	6	10	0	4	0	0	0
Shortness of breath	3	11	0	2	1	0	0
Wheezing	4	9	1	2	2	0	0
Tightness in chest	3	8	5	1	0	0	0
Cough	* 6	9	2	3	0	0	0
Sputum	1	11	1	2	0	0	0
Sore throat	2	12	0	2	0	0	0
Eye irritation	4	1	1	9	3	0	0
Nausea	1	14	0	0	0	0	0
Dizziness	2	14	0	0	0	0	0
Headache	1	11	0	3	0	0	0
Fatigue	0	11	0	3	0	0	0

\* No data for one subject.

2023373520

30-min intervals thereafter. Flow and volume signals were obtained from a Fleisch (No. 3) pneumotachograph and integrator, the corresponding loops being displayed on a Tectronix storage oscilloscope. At each test, the subject was seated and performed three maximum forced vital capacity (FVC) maneuvers. The loop with the largest FVC was analyzed for measurements including FVC, the 1-sec forced expiratory volume ( $FEV_{1.0}$ ), and maximum flow rates at 25% ( $\dot{V}_{max 25\%}$ ) and 50% ( $\dot{V}_{max 50\%}$ ) of vital capacity.

**Heart rates.** The electrocardiogram was monitored by a Sanborn 500 Visicardiette recorder throughout exposure, using chest leads fixed in the CM<sub>2</sub> position. Recordings were made at 10, 20, 40, 50, 70, 80, 100, and 110 min for the purpose of counting heart rates.

**Symptoms.** Subjects were asked to describe the symptoms they anticipated prior to entering the smoke-filled chamber. At the end of exposure, they were handed a list of 12 possible symptoms, and were required to rate each on a 6-point scale, ranging from absent (0) through trace (1), mild (2), moderate (3), severe (4), and incapacitating (5).

## RESULTS

### Symptoms

The number of symptoms reported on the questionnaire were somewhat greater than the reactions anticipated by the subjects prior to exposure (Table 3). The biggest discrepancy was for eye irritation, marked as present by all except one subject on the final questionnaire, but anticipated by only 4 of 13 subjects.

The commonest anticipated complaints were cough and nasal discharge or stuffiness. Shortness of breath, wheezing, or tightness in the chest were expected by only five of the group.

### Static Lung Volumes

Initial values for static lung volumes were on average close to normal predicted results (Table 1). At the end of the 2-hr sham exposure, RV and TLC tended to

TABLE 4  
EFFECTS OF SITTING IN EXPOSURE CHAMBER (SHAM EXPOSURE) AND "PASSIVE" EXPOSURE TO CIGARETTE SMOKE UPON STATIC LUNG VOLUMES\*

Variable	$C_{15}/C_0$ (%)	$E_{15}/C_0$ (%)	$E_{15}/C_{15}$ (%)
Relaxed vital capacity	99.8 ± 6.8	99.8 ± 5.3	98.0 ± 5.3
Residual volume	107.4 ± 19.2	109.6 ± 19.4	93.0 ± 16.4
Functional residual capacity	101.8 ± 9.3	103.9 ± 7.9	95.2 ± 13.1
Total lung capacity	102.8 ± 5.5	103.5 ± 3.4**	96.5 ± 4.6**

\* Data expressed as percentage of sham exposure at zero time ( $C_0$ ) or at end of sham exposure ( $C_{15}$ ). Mean ± SD.

P = 0.1.

P = 0.02.

P = 0.01.

2023379521



TABLE 3  
EFFECTS OF SITTING IN EXPOSURE CHAMBER (SHAM EXPOSURE) AND "PASSIVE" EXPOSURE TO CIGARETTE SMOKE UPON DYNAMIC LUNG VOLUMES\*

Variable	$C_{00}-C_0$ (%)	$E_0-C_0$ (%)	$E_{10}-C_{10}$ (%)	$E_{20}-C_{20}$ (%)	$E_{30}-C_{30}$ (%)	$E_{40}-C_{40}$ (%)
FVC	102.1 ± 5.4	101.3 ± 2.9	101.0 ± 7.4	100.1 ± 4.7	103.9 ± 6.5	100.6 ± 5.0
FEV <sub>1.0</sub>	105.9 ± 14.4	103.1 ± 11.6	102.1 ± 11.5	99.2 ± 12.1	102.1 ± 9.9	101.4 ± 7.9
$\dot{V}_{max 25.00}$	156.1 ± 121.0	101.6 ± 45.3	92.4 ± 45.6	86.6 ± 33.4	119.5 ± 56.0	124.8 ± 85.0
$\dot{V}_{max 50.00}$	114.4 ± 37.6	97.6 ± 27.8	96.4 ± 22.8	94.1 ± 17.5	102.9 ± 27.0	99.6 ± 26.9

\* Data expressed as percentage of sham exposure at zero time ( $C_0$ ) or at corresponding time in sham exposure ( $C_{10}$ ,  $C_{20}$ ,  $C_{30}$ ,  $C_{40}$ ). Mean ± SD.

†  $P < 0.1$ .

\*\*  $P < 0.05$ .

2023379522

increase, but not significantly so (Table 4). The FRC and TLC on the experimental day were larger than those measured prior to the sham exposure, the difference being particularly significant ( $P < 0.01$ ) for the TLC. These discrepancies were reversed over the 2-hr passive exposure to cigarette smoke, and at the end of the experiment the TLC was less than on the sham exposure day ( $P < 0.02$ ).

#### Dynamic Lung Volumes

The initial FVC was close to predicted normal values, but as would be anticipated there was a substantial impairment of  $FEV_{1.0}$  and  $\dot{V}_{max, 25\%VC}$  (Table 1). Two hours of sham exposure tended to increase late expiratory flow rates, the trend being of marginal significance ( $P < 0.1$ ) for  $\dot{V}_{max, 25\%VC}$  and  $\dot{V}_{max, 50\%VC}$  (Table 5). There was remarkably little change of dynamic volumes during passive cigarette smoke exposure relative to the corresponding sham exposure, the one statistically significant finding ( $P < 0.05$ ) being a small increase of FVC at 90 min of exposure.

#### Heart Rates

Heart rates did not change significantly over the 2-hr sham exposure. During passive exposure to cigarette smoke, average heart rates were always greater than 1/2 of the corresponding sham value, this difference being significant ( $P < 0.05$ ) in the 30th min of exposure.

#### Subjects Claiming Cigarette Smoke Sensitivity

Data were analyzed separately for the four subjects who anticipated the symptom of wheezing during passive cigarette smoke exposure, and the ten who did not anticipate this response. On the experimental day, the "sensitive" subgroup tended to an increase of residual volume, functional capacity, and total lung capacity relative to other subjects (Table 7). However, they showed a similar difference of behavior during the sham exposure, so that when each individual's sham exposure was used as the control data ( $E_{120}C_{120}$ ), residual volume, func-

TABLE 6  
EFFECT OF SITTING IN EXPOSURE CHAMBER (SHAM EXPOSURE) AND "PASSIVE" EXPOSURE TO CIGARETTE SMOKE ON HEART RATE\*

Time (min)	Sham exposure percentage $C_0$ (%)	Passive exposure, percentage of corresponding sham exposure $C_1$ (%)
0	100	102 ± 16
10	97 ± 5	104 ± 11
20	96 ± 7	105 ± 14
30	98 ± 8	102 ± 8
40	98 ± 8	103 ± 10
50	98 ± 8	102 ± 9
60	93 ± 8	106 ± 11
80	96 ± 7	102 ± 15
100	97 ± 9	104 ± 19

\* Data expressed as percentage of sham exposure at zero time ( $C_0$ ) or at corresponding time  $C_1$  during sham exposure ( $C_0 = 100$ ,  $n = 10$ , mean ± SD).

$P < 0.05$ .

2023375523

TABLE 7  
RESPONSE OF SUBJECTS ANTICIPATING WHOLEZING ("SENSITIVE"  $N = 4$ ) RELATIVE TO  
REMAINDER OF GROUP (OTHER, 0). (MEANS FOR EACH CATEGORY)

	$E_{120} E_{120}$ (%)		$C_{120} C_{120}$ (%)		$E_{120} C_{120}$ (%)	
	(S)	(O)	(S)	(O)	(S)	(O)
Relaxed vital capacity	98	98	100	100	101	97
Residual volume	100	91	120	100	85	97
Functional residual capacity	97	94	107	102	92	96
Total lung capacity	99	94	105	102	97	96
FVC	99	102	103	102	100	101
FEV <sub>1.0</sub>	100	106	103	107	107	99
$V_{max 25-75}$	127	153	121	170	103	97
$V_{max 50-90}$	95	125	104	119	100	99

\* Comparison of preexposure and 120 min of exposure ( $E_{120} E_{120}$  %). Corresponding sham experiment ( $C_{120} C_{120}$  %). Comparison of experimental and sham exposure at 120 min ( $E_{120} C_{120}$  %).

\* Omitting one subject with very high value (mean for all subjects = 133).

\*  $P < 0.1$ .

\*\*  $P < 0.05$ .

\*\*\*  $P < 0.01$ .

tional residual capacity, and total lung capacity on the experimental day were reduced at least as much in the "sensitive" subjects as in the remainder of the sample.

Taking data for the experimental day, the "sensitive" subgroup tended to a decline of dynamic lung volumes relative to the behavior of the other subjects, the discrepancy approaching significance for the  $V_{max 25-75}$  (Table 7). Again, there was a tendency for a similar discrepancy between the two subgroups on the sham exposure day, so that when the individual's sham exposure data was used as a control ( $E_{120} C_{120}$  %), all values for "sensitive" and "other" subjects agreed to within 5-6%; the only statistically significant difference was a small increase of FEV<sub>1.0</sub> in the "sensitive" subjects.

## DISCUSSION

### Behavior Relative to Nonasthmatic Subjects

The frequency and severity of most symptoms was much as reported for normal subjects exposed to a comparable concentration of cigarette smoke (Pimm *et al.*, 1978; Shephard *et al.*, 1979a) (Table 8), with the exception that almost a half of the asthmatic sample complained of wheezing and tightness in the chest. Coughing was more severe in the normal subjects, although this is probably related to the fact that they performed intermittent exercise and thus received a greater dose of smoke than the asthmatic individuals. The latter were observed while sitting at rest because of the problem that exercise would of itself have provoked bronchospasm in this group.

The physiological changes observed in normal subjects during smoke exposure, although occasionally reaching conventional levels of statistical significance, were of doubtful biological importance (Pimm *et al.*, 1978; Shephard *et al.*, 1979a).

2023379524

TABLE II  
A COMPARISON OF SYMPTOMS IN NORMAL AND IN ASTHMATIC SUBJECTS DURING "PASSIVE" EXPOSURE TO CIGARETTE SMOKE\*

Symptom	Percentage affected			Average symptom score	
	Normal subjects		Asthmatic subjects rest (%)		
	Rest (%)	Intense exercise (%)		Normal subjects Intense exercise	Asthmatic subjects rest
Nasal discharge or stiffness	35	33	28	0.33	0.61
Shortness of breath	15	17	21	0.33	0.30
Wheezing	10	0	36	0.00	0.84
Tightness in chest	5	0	43	0.00	0.46
Cough	45	58	36	1.00	0.54
Sputum	40	8	21	0.00	0.31
Eye irritation	95	92	93	2.67	1.92
Nausea	10	0	0	0.00	0.00
Dizziness	10	25	0	0.42	0.00
Headache	15	25	21	0.58	0.46
Fatigue	0	17	21	0.33	0.46

\* Percentage of subjects reporting the symptom. Average symptom score based on the reported intensity of a given symptom (ranging from 0 = absent to 3 = incapacitating).

2023379525

Findings included some increase of heart rate and respiratory minute volume, probably of emotional origin, a tendency of increase in functional residual capacity and residual volume in some experiments, and small decreases of dynamic lung volumes. The asthmatic subjects also showed emotional reactions to the cigarette smoke, including the tachycardia, and possibly the preexposure increase of FRC and TLC. Taking the group as a whole, there was no evidence of impairment of dynamic lung volumes during the passive cigarette exposure. It might be argued that emotional reactions to the smoke-filled chamber were sufficient to mask such a response. However, we did not form the impression that subjects were unduly alarmed by the experiment, and the observed tachycardia after 2-hr passive smoke exposure was slight. We did not measure serum or urinary nicotine levels, but again the absence of any marked tachycardia speaks against a nicotine-mediated release of epinephrine. Russell and Feyerabend (1975) concluded that the rapid excretion of nicotine made a systemic pharmacological action an improbable sequel to sustained passive cigarette smoke exposure. We would thus conclude that there was little likelihood of a sufficient increase in sympatho-adrenal activity, emotional or pharmacological, to counteract cigarette smoke-induced bronchospasm.

The most interesting observation is the small decrease of TLC as measured by helium dilution (Table 4). This could imply an effect of the smoke upon the small airways, with an increase of gas trapping, and it would be worthwhile to extend observations using some more specific measures of small airway function such as helium flow-volume curves.

#### *Sensitive Subjects*

Although several of the asthmatic subjects claimed wheezing and tightness in the chest would result from passive exposure to cigarette smoke, the physiological data give little support to the concept of a subgroup with particular sensitivity.

On the experimental day, the group claiming sensitivity showed a tendency of increase in static lung volumes, and a decrease in dynamic volumes. However, changes were of almost equal magnitude during the sham exposure. We may thus hypothesize that the observed reactions are due to the suggestibility of the subjects rather than a pharmacological or allergic reaction to cigarette smoke. In support of this view, the only significant difference in the "sensitive" group was a greater FEV<sub>1.0</sub> relative to the corresponding time in the control exposure, presumably due to greater sympathetic activation and/or arousal in the smoke-filled environment.

#### *Implications for Air Quality Legislation*

While there may be valid grounds for controlling the cigarette smoke concentration in "public" air (Shephard *et al.*, 1979a), the present data offer little support to the view that asthmatic subjects need special consideration in this regard. Complaints of tightness in the chest and wheezing were more frequent than in the general population, but the only statistically significant physiological response was a very small decrease of TLC. Further, this change was not significantly greater in those complaining of chest symptoms. The subjective reactions thus

2023379526

seem but one more manifestation of annoyance, almost universal at the concentration evaluated.

~~It is possible that some subjects might have been~~  
~~exposed at higher smoke concentrations.~~ Nevertheless, the value used is the highest likely figure to which an asthmatic subject will be exposed (Sehben *et al.*, 1977), and indeed with adequate ventilation smoke concentrations can be held to substantially lower figures.

We would thus conclude that the specific sensitivity of asthmatic subjects is not a major consideration when determining air quality criteria for rooms contaminated by cigarette smoke.

#### ACKNOWLEDGMENT

This research was supported in part by a research grant from Health and Welfare, Canada.

#### REFERENCES

- Basu, P. K., Pimm, P. E., Shephard, R. J., and Silverman, F. (1978). The effect of cigarette smoke on the human tear film. *Canad. J. Ophthalmol.* 13, 22-26.
- Blue, J. A. (1970). Cigarette asthma and tobacco allergy. *Ann. Allergy* 28, 110-115.
- Pimm, P., Shephard, R. J., and Silverman, F. (1978). Physiological effects of acute passive exposure to cigarette smoke. *Arch. Environ. Health* 33, 201-203.
- Russell, M. A. H., and Feyerabend, C. (1975). Blood and urinary nicotine in non-smokers. *Lancet* 1, 179-181.
- Savel, H. (1970). Clinical hypersensitivity to cigarette smoke. *Arch. Environ. Health* 21, 146-148.
- Schilling, R. S. F., Letai, A. D., Hui, S. L., Beck, G. J., Schoenberg, J. B., and Bouhuys, A. (1977). Lung function, respiratory disease, and smoking in families. *Amer. J. Epidemiol.* 106, 274-283.
- Sehben, J., Pimm, P., and Shephard, R. J. (1977). Cigarette smoke in enclosed public facilities. *Arch. Environ. Health* 32, 53-58.
- Shephard, R. J., and LaBarre, R. (1978). Attitudes of the public towards cigarette smoke in public places. *Canad. J. Publ. Health* 69, 302-310.
- Shephard, R. J., Collins, R., and Silverman, F. (1979a). Responses of exercising subjects to acute "passive" cigarette smoke exposure. *Environ. Res.* 19, 279-291.
- Shephard, R. J., Ponsford, L., LaBarre, R., and Basu, P. K. (1979b). Subjective reactions to passive cigarette-smoke exposure. Effect of cigarette smoke on the eyes and airways. *Int. Arch. Occup. Environ. Health* 43, 135-144.
- Speer, F. (1968). Tobacco and the non-smoker. A study of subjective symptoms. *Arch. Environ. Health* 16, 443-446.
- Wynder, E. L., and Hoffman, D. (1967). "Tobacco and Tobacco Smoke. Studies in Experimental Carcinogenesis." Academic Press, New York.
- Zussman, B. M. (1970). Tobacco sensitivity in the allergic patient. *Ann. Allergy* 28, 371-377.

2023373527

2023373528

Dahms, T.E., Bolin, J.F., Slavin, R.G. "Passive Smoking: Effects on Bronchial Asthma" Chest 80: 530-534, 1981.

ABSTRACT. Ten patients with bronchial asthma and ten control subjects were exposed to sidestream cigarette smoke (passive smoking) for one hour in an environmental chamber. All subjects showed the same increase in carboxyhemoglobin as a result of the exposure: 0.40 percent. The asthmatic group demonstrated a significant linear decrease in pulmonary function during this exposure. After one hour of smoke, FEV1 decreased 21.4 percent, FEF25-75% decreased 19.2 percent, and FVC decreased 20.0 percent in the asthmatic patients. These alterations were readily reversible in all subjects when given inhalations of metaproterenol following the exposure. The control subjects showed no change in pulmonary function when exposed to identical conditions. These data show that nonsmokers with bronchial asthma are at risk when exposed to sidestream cigarette smoke in an environmental chamber.

2023373529





## Passive Smoking

### Effects on Bronchial Asthma\*

T. E. Dahms, Ph.D.; J. F. Bolin, M.D.; and R. G. Slavin, M.D.

Ten patients with bronchial asthma and ten control subjects were exposed to sidestream cigarette smoke (passive smoking) for one hour in an environmental chamber. All subjects showed the same increase in carboxyhemoglobin as a result of the exposure: 0.40 percent. The asthmatic group demonstrated a significant linear decrease in pulmonary function during this exposure. After one hour of smoke, FEV<sub>1</sub> decreased 21.4 percent, FEF<sub>25-75%</sub> decreased 19.2 percent, and FVC

decreased 20.0 percent in the asthmatic patients. These alterations were readily reversible in all subjects when given inhalations of metaproterenol following the exposure. The control subjects showed no change in pulmonary function when exposed to identical conditions. These data show that nonsmokers with bronchial asthma are at risk when exposed to sidestream cigarette smoke in an environmental chamber.

#### METHODS

To determine more objectively the effects of passive smoking on persons who have a reactive respiratory tract, ten patients with bronchial asthma and ten control subjects were exposed to mechanically produced cigarette smoke in an environmental chamber. The control subjects were healthy, nonsmoking men and women 24 to 53 years old, who volunteered from the medical community. Five of the control subjects complained of general irritability when exposed to passive smoking environments. Nonsmoking asthmatic subjects, recruited from the St. Louis University Hospital Allergy Clinic, were men and women ranging in age from 18 to 26 years. Five of the asthmatic patients were included because they reported specific complaints when exposed to cigarette smoke; the remaining asthmatic patients were recruited at random. All subjects were fully informed, and the guidelines of informed consent were followed.

All asthmatic subjects had a previous medical history of bronchospasm and a positive methacholine challenge test. A positive methacholine test consisted of at least 20 percent fall in FEV<sub>1</sub> as a result of inhaling a nebulized solution of 25 mg/ml or less of methacholine. A graded methacholine challenge test<sup>4</sup> was carried out at least one week before the smoke exposure on only the asthmatic subjects.

The general protocol consisted of an initial history and physical examination of the subjects to ensure that the subjects were asymptomatic. The asthmatic subjects continued taking their medication but refrained from using any bronchodilators for four hours before the experiment. Then the preexposure blood sample was drawn for carboxyhemoglobin (COHb) analysis. The subjects entered the chamber, and the control pulmonary function tests were performed after 15 minutes. The smoke generator was started, and at 15-minute intervals the pulmonary tests were repeated. Since all of the testing was carried out in the chamber, the subjects remained in the chamber for the entire 60 minutes of the exposure. After the final pulmonary function tests at 60 minutes, a second blood sample was collected for COHb analysis.

The environmental chamber used was 30 m<sup>3</sup> in volume,

The evidence regarding cigarette smoke exposure producing pulmonary changes leading to bronchospasm in asthmatic patients is only anecdotal. Speer<sup>1</sup> reported results of an investigation using a questionnaire given to allergic and nonallergic patients detailing their reactions to cigarette smoke. When exposed to passive smoking conditions, the allergic, nonsmoking subjects reported a greater incidence of eye irritation, nasal symptoms, cough, wheezing, sore throat, and hoarseness than did the nonallergic, nonsmoking subjects. The available data suggest an increased sensitivity of patients with bronchial asthma to cigarette smoke; however, there is currently no objective information to support the subjective data of Speer.<sup>1</sup>

Passive smoking, the inhalation by nonsmokers of the combustion products of cigarettes from sidestream smoke and exhaled smoke, is a common form of indoor air pollution. Long-term passive exposure of both adults<sup>2</sup> and children<sup>3</sup> to cigarette smoke can lead to a significant reduction in the function of small airways. However, if any group would be at immediate risk from cigarette exposures, it would be one whose members have an irritable airway. This report concerns the acute pulmonary responses of bronchial asthmatic patients and control subjects in a passive smoking environment. These experiments were carried out in an attempt to determine whether a factual basis exists for the anecdotal and subjective information reported by Speer<sup>1</sup> regarding bronchial asthmatic patients.

\*From the Departments of Physiology and Internal Medicine, St. Louis University School of Medicine, St. Louis. Reprint requests: Dr. Slavin, Internal Medicine/Allergy, 3553 Vista Avenue, St. Louis 63104.

with precise humidity, temperature, air flow, and air turnover control enabling control over the exposure environment. Other conditions used were a temperature of 21 °C, relative humidity of 50 percent and an air turnover of once every 12 minutes. The smoke was produced from cigarettes (15 mg of tar and 0.15 mg of nicotine) smoked with a 30-ml puff volume at one cycle per minute to a butt length of 30 mm. The passive smoke concentration was estimated from the rate of production of carbon monoxide (CO) and particulates in combination with the room volume and the air turnover rate.<sup>8</sup> The room levels of CO were confirmed by the increase in COHb of each of the subjects. Preexposure and postexposure venous blood samples were drawn, and the hemoglobin and CO content of the samples were precisely determined.<sup>9</sup> All subjects averaged an increase of 0.40 percent COHb during the exposure, which, according to the model of Jones and Fagen<sup>7</sup> showed that the environmental CO concentration averaged between 15 and 20 ppm over the 60-minute exposure. The particulate matter in the atmosphere of the chamber was probably less than what would be expected, owing to the precipitating action of the circulating fans and the refrigeration coils in the chamber. No measurement of particulate matter was made.

The asthmatic patients were given metaproterenol (Aloper) from an inhaler immediately following the postexposure blood sample and were removed from the chamber. Fifteen minutes later pulmonary function tests were repeated.

All pulmonary function tests were performed on a waterless spirometer (Jones-Pulmonor). Only three parameters were assessed: forced vital capacity, FVC; forced expiratory volume after 1 second, FEV<sub>1</sub>; and mean forced expiratory flow during the middle half of the FVC, FEF<sub>25-75%</sub>. At each measurement period three repetitions were carried out and the highest values were used in the analyses.<sup>8</sup> A simple spirometric test was chosen to minimize the interference of the testing procedure with the potential physiologic changes due to the cigarette smoke. All of the patients had become thoroughly familiar with the apparatus during routine testing in the clinic, which reduced to a minimum problems with

patient compliance and task learning.

All data were analyzed via analysis of variance, and significance for each parameter at any given time was determined via Tukey's *t* test. Levels of significance were determined as a result of smoke exposure by using a within-group design: asthmatic values during smoke exposure were compared with asthmatic control values (paired analysis).

## RESULTS

The asthmatic subjects showed a highly significant decrease in pulmonary function throughout the exposure to the sidestream cigarette smoke (Table 1). The FVC decreased significantly after 15 minutes of exposure ( $P < 0.01$ ), from 4,490 ml to 3,135 ml. After one hour of smoke exposure the FVC had decreased on an average of 650 ml or 20.0 percent. The control subjects showed no change in FVC as a result of exposure to the same conditions. In the asthmatic patients the FEV<sub>1</sub> fell throughout the exposure, but did not become statistically significant until 30 minutes. After 60 minutes FEV<sub>1</sub> had fallen 200 ml (2.9 percent). In the asthmatic subjects, whereas the controls showed a slight but insignificant increase in FEV<sub>1</sub> after 60 minutes of smoke exposure. All but one of the asthmatic patients had reductions in both FVC and FEV<sub>1</sub>. The FEF<sub>25-75%</sub> in the asthmatic group also decreased throughout the exposure to the sidestream cigarette smoke, but the decrease did not reach statistical significance until 30 minutes ( $P < 0.05$ ). In the asthmatic group the FEF<sub>25-75%</sub> decreased from 4.09 L/sec before exposure to 1.61 L/sec (19.2 percent) after 60 minutes.

The decrease in FEF<sub>25-75%</sub> may have been due

Table 1—Group Mean Data of Pulmonary Response to Passive Smoking\*

Test	Duration of Passive Smoke Exposure					15 min After Bronchodilator
	0	15 min	30 min	45 min	60 min	
<b>FVC</b>						
Control group	4,490 (±291)	4,550 (±304)	4,490 (±290)	4,530 (±292)	4,530 (±292)	
% Change		4.3	0	0.9	0.9	
Asthmatic group	3,395 (±190)	3,135 (±185)	3,005 (±190)	2,820 (±192)	2,715 (±217)	3,475 (±354)
% Change		-7.45‡	-10.9‡	-16.2‡	-20.0‡	+2.4
<b>FEV<sub>1</sub></b>						
Control group	3,625 (±222)	3,765 (±204)	3,705 (±199)	3,795 (±195)	3,815 (±204)	
% Change		3.9	4.7	4.7	5.2	
Asthmatic group	2,475 (±173)	2,285 (±176)	2,190 (±172)	2,060 (±198)	1,955 (±175)	2,336 (±221)
% Change		-8.6	-12.9‡	17.5‡	-21.4‡	-5.6
<b>FEF<sub>25-75%</sub></b>						
Control group	4.09 (±.53)	4.11 (±.36)	4.15 (±.30)	4.16 (±.30)	4.18 (±.31)	
% Change		0.5	1.5	1.7	2.2	
Asthmatic group	1.95 (±.24)	1.77 (±.26)	1.74 (±.26)	1.64 (±.28)	1.61 (±.28)	2.03 (±.34)
% Change		10.9	-10.9‡	-18.4‡	-19.2‡	-4.1

\*Values given are ± SEM. All values in asthmatic group are significantly different from control values at all measurement periods ( $P < 0.01$ ).

†Values significantly different from preexposure ( $P < 0.05$ ).

‡Values significantly different from preexposure ( $P < 0.01$ ).

Table 2—Subject Description and Baseline Pulmonary Function Values Before Exposure to Passive Smoking\*

Group	N	Age Range, yr	VC		FEV <sub>1</sub>		FEF25-75%	
			Mean	% Pred	Mean	% Pred	Mean	% Pred
Control subjects	10	24-53	4,490 ±291	93.0	3,625 ±222	97.5	4.09 ±0.05	104.9
Asthmatic patients	10	16-39	3,395† ±190	79.2	2,475† ±173	73.7	1.95† ±0.24	51.5

\*Values ± SEM.

†Value significantly different from controls at  $P < 0.05$ .

in part to decreases in lung volume, since the FVC also fell. However, on an individual-by-individual basis, the changes in FEF25-75% did not correlate in all cases with a decrease in FVC. For example, the 60-minute exposure values of FVC in two of the asthmatic subjects fell 36 percent and 22 percent, but their respective FEF25-75% fell only 4 percent and 6 percent. However, the three largest responders in FEF25-75%, 44, and 25 percent, also had FVC decreases of 33, 23 and 24 percent respectively. Two of the subjects had greater percentage decreases in FEF25-75% than in FVC, the inverse of the other eight subjects. Therefore, not all subjects showed the same pattern of pulmonary responses to the smoke exposure.

The asthmatic subjects' preexposure pulmonary function values were considerably lower than those values of the control subjects (Table 2). The average values for the asthmatic subjects also were less than the predicted normal values<sup>9</sup> for the measurements used in the study: FVC, 79.2 percent; FEV<sub>1</sub>, 73.7 percent; and FEF25-75%, 51.5 percent of predicted. This is in contrast to the control subjects, whose values all were within 93 to 104 percent of predicted values. Therefore, the decreases in pulmonary function in the asthmatic subjects as a result of the passive smoking presented further risk to already compromised respiratory system.<sup>4</sup> One asthmatic patient had an audible wheeze at 60 minutes of exposure.

Following the exposure to the passive smoking conditions, the asthmatic patients were given metaproterenol via an inhaler. Fifteen minutes later the pulmonary function tests were performed. Two of the asthmatic subjects improved with the bronchodilator but did not return to their preexposure status; however, the remaining asthmatic patients returned to baseline or above. The subjects who did not return to baseline had the greatest decreases in FEV<sub>1</sub> and FVC and were among the highest responders in FEF25-75%. The group responses showing a return to baseline values are shown in Table 1.

All subjects, control and asthmatic, incurred the

same subjective degree of eye and nasal irritation. Both the control and asthmatic groups increased their COHb concentrations to the same extent as a result of the exposure (Table 3). The control group's COHb increased 0.43 percent, from 0.62 percent to 1.05 percent ( $P < 0.01$ ), and the asthmatic group increased 0.38 percent from 0.82 to 1.20 percent ( $P < 0.01$ ). There was no statistical difference in the elevation in COHb between the groups, suggesting identical exposure for each group. There was also no relationship found between the slight differences in individual increments in COHb and their corresponding decrements in pulmonary function.

The methacholine challenge test results indicate that this group of asthmatic patients was moderately sensitive to methacholine. Five of the asthmatic subjects responded with a 20 percent decrease in FEV<sub>1</sub> (threshold criterion) with the lowest dose of 0.075 mg/ml in the nebulizer; one responded at 0.15 mg/ml, two at 0.62 mg/ml, and two at 1.25 mg/ml. The dose required for confirmation of asthma is 25 mg/ml, a value considerably above that for anyone in this group of asthmatic patients. No significant relationships were found between methacholine sensitivity and pulmonary response, primarily because of the small size of the sample. Seven of the subjects show such a relationship, but the inclusion of the other three skew the data and remove any significance.

### Discussion

The evidence from this investigation clearly demonstrates that passively encountered cigarette smoke produces an increase in airway resistance in patients

Table 3—Increases in Carboxyhemoglobin as a Result of Exposure to Sidestream Cigarette Smoke\*

Group	Preexposure	% COHb at 60 min of Exposure	Increase, %
Control subjects	0.62% ± 0.08	1.06† ± 0.08	0.43
Asthmatic patients	0.82% ± 0.10	1.20† ± 0.09	0.38

\*Values ± SEM.

†Values significantly different from preexposure values where  $P < 0.01$ .

with bronchial asthma.<sup>10</sup> This increase in resistance was demonstrated by a significant decrease in both FEV<sub>1</sub> and FEF<sub>25-75%</sub> after 30 minutes of exposure to the cigarette smoke. The decrease in pulmonary function was linear over the 30-minute exposure, reaching a total decrement of approximately 20 percent of control values in all parameters at 60 minutes. The identical conditions produced no measurable effects in control subjects.

In an attempt to explain these results, comparisons can only be made with the effects of active smoking, since so little information is available regarding acute physiologic responses to passive smoking. The difference between the two conditions might be one merely of degree, *i.e.*, smoke concentration. Nadel and Comroe<sup>11</sup> demonstrated that airway resistance increased immediately when healthy subjects smoked a single cigarette. This bronchoconstriction was thought to be due to a reflex initiated by the particulate matter in the smoke.<sup>10,11</sup> The increase in airway resistance seen in the asthmatic subjects in this study required 30 minutes of inhalation of the diluted sidestream smoke to produce significant decrements in the pulmonary parameters used to assess airway resistance. When a cigarette is burned under the conditions used in these experiments, the sidestream smoke will contain more than three times the particulate mass of the mainstream smoke. The mainstream smoke inhaled in active smoking is diluted in only the tidal volume before reaching the airways, whereas the sidestream smoke particles are diluted in the volume of the entire room. This results in a 10<sup>3</sup>-fold difference in the inhaled particulate concentration between active smoking and passive smoking. If the particulate matter were the stimulus for the responses seen in the asthmatic subjects, their airways would have to be considerably more sensitive to particulates than the controls.

The bronchoconstriction resulting from the active smoking of one cigarette in healthy nonsmokers is thought to be a reflex<sup>10,12</sup> mediated via particulates stimulating parasympathetic pathways. Bronchial asthmatic patients are characterized by hyperactivity of the bronchi to various stimuli resulting in increased airway resistance that is manifested in the extreme as paroxysmal and reversible wheezing and dyspnea. The specific mechanisms that can lead to bronchial asthma are unknown, but several factors can definitely cause a significant increase in airway resistance in asthmatic patients. Inhaled aerosols of histamine, acetylcholine, methacholine, and dust particles cause much greater bronchoconstriction in asthmatic patients than in normal subjects.<sup>4</sup> Asthmatics with their obstructive type of ventilatory

function have been found to have a larger than normal intrapulmonary deposition of inhaled particulates, and the range of sites of deposition is shifted proximally.<sup>13</sup> Therefore, the asthmatic subjects probably responded to the passive smoke because they had an increased sensitivity of bronchiolar receptors and perhaps a greater number of particles deposited on the hypersensitive airways.

Although particulates have been implicated<sup>10,12</sup> as the primary stimulus, the gaseous phase cannot be completely ruled out as a possible causative agent in the response of the airways in the bronchial asthmatic patients to passive smoking.

The effects reported here were not influenced by the maximal inspiratory and expiratory maneuvers used in the testing procedure. The subjects, control and asthmatic groups, repeated the FVC maneuvers three times with a 15- to 30-second interval between maneuvers. If any of these influences had played a role, a definite order effect would have been seen in the FEV<sub>1</sub> and FEF<sub>25-75%</sub> values. No order effect was seen, suggesting that deep inspiration and expiration had no effect on the results of this investigation.

We were not able to exclude the possibility that these changes in pulmonary function were emotionally related to cigarette smoke. Horton et al<sup>14</sup> have shown a high correlation between emotional responses in specific airway conductance and sensitivity to methacholine or histamine. The emotional response described by Horton et al<sup>14</sup> was manifested immediately, whereas the subjects exposed to the sidestream cigarette smoke in the present study did not show a significant change in airway resistance until 30 minutes of exposure. Although an emotional component could have been present, increasing with duration of exposure, the portion of the response due to emotion cannot be determined. Also the range of methacholine sensitivity in the asthmatic patients in this study who specifically complained of cigarette smoke irritation was quite large, *i.e.*, it was not the subjects most sensitive to the methacholine who felt particularly bothered by the smoke.

The exposure conditions were representative of moderate environments, and all the asthmatic subjects felt that they had been exposed to similar environmental conditions in their lives. However, many asthmatic patients avoid such situations. The atmospheric carbon monoxide concentration range of 15 to 20 ppm is within the range of hourly averages reported<sup>15,17</sup> for taverns and nightclubs of 3 to 29 ppm. Some hourly averages for such locations occasionally reached 36 to 42 ppm. The air turnover in the environmental chamber used for these experiments is similar to that found in and recommended

for various environments.<sup>18</sup>

Long-term exposure to environmental cigarette smoke results in changes in pulmonary function of nonsmokers suggestive of small airway disease.<sup>2</sup> These effects, however, were measured after a minimum of 20 years of exposure of the subjects to a smokey environment. The passive smoking environment may pose a more immediate threat to persons with a reactive respiratory tract. In 1974 it was recommended that reactive persons in the population be studied because adverse effects of environmental tobacco smoke may occur at very low concentrations among atopic patients and persons who otherwise have a reactive respiratory tract.<sup>18</sup> The results of this initial investigation indicate that patients with bronchial asthma do respond adversely when actively exposed to environmental cigarette smoke. Aronow<sup>19</sup> recently reported that under conditions of acute exposure to smoke, some angina patients are also at additional risk of suffering anginal attacks. It is still to be determined to what extent these results can be generalized to the entire groups of people with these chronic diseases.

**ACKNOWLEDGMENT:** The authors would like to thank Dr. S. M. Ayres for his helpful suggestions throughout this project and Dr. C. J. Gaebelin for his help with the statistical analysis.

#### REFERENCES

- 1 Speer F. Tobacco and the nonsmoker. *Arch Environ Health* 1968; 16:443-46
- 2 White JR, Froeb HF. Small airways dysfunction in nonsmokers chronically exposed to tobacco smoke. *N Engl J Med* 1980; 302:720-23
- 3 Tager IB, Weiss ST, Rosem B, Speizer FE. Effect of parental cigarette smoking on the pulmonary function of children. *Am J Epidemiol* 1979; 110:15-28
- 4 Parker, CD, Bilbo RE, Reed CE. Methacholine aerosol as test for bronchial asthma. *Arch Intern Med* 1965; 115:452-58
- 5 Hoegg UR. Cigarette smoke in closed spaces. *Environ Health Perspect* 1972; 2:117-28
- 6 Dahms TE, Horvath SM. Rapid, accurate technique for determination of carbon monoxide in blood. *Clin Chem* 1974; 20:533-37
- 7 Jones RM, Fagan R. Carboxyhemoglobin in nonsmokers. *Arch Environ Health* 1975; 30:184-89
- 8 Nathan SP, Lebowitz MD, Knudson RJ. Spirometric testing: number of tests required and selection of data. *Chest* 1979; 76:384-88
- 9 Coates JE. Lung function. Philadelphia; FA Davis, 1968; 374-5
- 10 Nadel JA, Comroe JH, Jr. Acute effects of inhalation of cigarette smoke on airway conductance. *J Appl Physiol* 1961; 16:713-16
- 11 Widdicombe JB, Kent DC, Nadel JA. Mechanism of bronchoconstriction during inhalation of dust. *J Appl Physiol* 1962; 17:613-16
- 12 Sterling GM. Mechanism of broncho-constriction caused by cigarette smoking. *Br Med* 1967; 3:275-77
- 13 Muir DCF. Tobacco smoke inhalation. *Scand J Respir Dis Suppl* 1974; 91:44-46
- 14 Horton DJ, Suda WL, Kinsman RA, Souhrada J, Spector SL. Bronchoconstrictive suggestion in asthma: a role for airways hyperreactivity and emotions. *Am Rev Respir Dis* 1978; 1029-38
- 15 Sebben J, Pimm P, Shephard RJ. Cigarette smoke in enclosed public facilities. *Arch Environ Health* 1977; 32:53-37
- 16 Chappel SB, Parker RJ. Smoking and carbon monoxide levels in enclosed public places in New Brunswick. *Can J Public Health* 1977; 68:159-61
- 17 Hinds WC, First MW. Concentrations of nicotine and tobacco smoke in public places. *N Engl J Med* 1975; 292:844-48
- 18 Corn M, Kilburn KH, Rylander R. Workshop summary and recommendation from environmental tobacco smoke effects on the non-smoker. *Scand J Respir Dis Suppl* 1974; 91:88-90
- 19 Aronow WS. Effect of passive smoking on angina pectoris. *N Engl J Med* 1978; 299:21-24

**2023379535**

## The Thoracic Society of Australia

Annual Scientific Meeting, May 1983

The following are abstracts of papers presented at the Annual Scientific Meeting of the Thoracic Society of Australia held in Perth, Western Australia, 2-4 May, 1983.

### NEUTROPHIL CHEMOTACTIC ACTIVITY FOLLOWING THE INHALATION OF ULTRASONICALLY NEBULISED WATER

R. SHAW, S. DURHAM, P. TORZILLO, R. E. SCHOEFFEL,  
S. D. ANDERSON AND A. B. KAY

*Department of Thoracic Medicine, Royal Prince Alfred Hospital,  
Sydney, Australia and Department of Allergy and Clinical  
Immunology, Cardio-Thoracic Institute, London, England*

An increase in serum of a high molecular weight neutrophil chemotactic factor (NCF) has been described in patients with exercise and allergen induced asthma. The increase in NCF after exercise has been shown to be inhibited by sodium cromoglycate suggesting that NCF may reflect mast-cell activation.

We carried out a study in seven asthmatics and five normal subjects to determine if the change in airways resistance following the inhalation of ultrasonically nebulised water (UNH<sub>2</sub>O) is also associated with an increase in neutrophil chemotactic activity.

Eight ml of blood was collected from an antecubital fossa vein and allowed to clot on glass for three hours at 4°C. The serum was collected and heated at 56°C for 30 min, then stored at -80°C until analysis. Samples were collected at rest, immediately at the end of challenge, 5, 10, 15, 30 and 60 min. later. Neutrophil chemotactic factor activity was assayed in a modified Boyden chamber in which a micropore filter separates a neutrophil suspension from a 20 percent dilution of test serum. Following incubation the filter is removed and examined by microscopy for evidence of neutrophil migration.

A MistOgen Ultrasonic Nebuliser (EN143A, California) which delivers approximately 1 ml of water per 10 L of aerosol inhaled was used for the challenge. Forced expiratory volume in one second (FEV<sub>1</sub>), forced expiratory flow rate over the middle half of the vital capacity (FEF<sub>25-75</sub>) and the flow rate at 50% of the vital capacity (V50) were measured using a Cavitron (SC-20 Spirometer, Anaheim, California).

Measurements were made in triplicate at rest and 30 sec. after the inhalation of a known volume of nebulised H<sub>2</sub>O. The mean  $\pm$  SD FEV<sub>1</sub> at rest (expressed as a percentage of the predicted value) was 80.2%  $\pm$  21.8 for the asthmatics and 104.3%  $\pm$  19 for the normal subjects. Following the water challenge the mean maximum reduction in each measurement was calculated and expressed as a percentage of the pre-challenge value. For the seven asthmatics the mean maximum fall  $\pm$  1 SD for FEV<sub>1</sub> was 41.6%  $\pm$  11.5, for FEF<sub>25-75</sub> 46.4%  $\pm$  4.2 and for V50 51.0%  $\pm$  5.7. The mean  $\pm$  1SD delivered dose of H<sub>2</sub>O required to induce the maximum recorded change in FEV<sub>1</sub> was 6.8 ml  $\pm$  5.5. For the normal subjects the reduction in FEV<sub>1</sub>, FEF<sub>25-75</sub>

and V50 was less than 20% of the pre-challenge level after the inhalation of 33 ml of H<sub>2</sub>O.

There was no significant difference in the pre-challenge levels of neutrophils per 10 high power fields (N10HPF) between the asthmatic and normal subjects. In the 30 min after challenge there was a mean  $\pm$  1 SD maximum increase in N10HPF of 179  $\pm$  118 in the asthmatics and 42  $\pm$  15.5 in the normal subjects ( $p < 0.05$ ). Sixty minutes after challenge the values for N10HPF had returned to within 8% of the resting levels.

We concluded that the airways obstruction induced by the inhalation of UNH<sub>2</sub>O is associated with an increase in serum neutrophil chemotactic activity.

### RELATIONSHIP BETWEEN AIRWAY SMOOTH MUSCLE VOLUME AND HISTAMINE REACTIVITY IN VIVO/IN VITRO IN HUMAN AIRWAYS

C. L. ARMOUR, N. M. LAZER, R. R. SCHELLENBERG,  
J. C. HOGG AND P. D. PARE

*UBC Pulmonary Research Laboratory, Vancouver, Canada*

Non specific airway hyperreactivity is now recognised as a characteristic feature of human asthma. Alteration in the smooth muscle within the airways has been suggested as the basis of hyperreactivity.

The present study examined lung function and nonspecific bronchial reactivity in 12 patients with chronic obstructive lung disease prior to resection of lung tissue for carcinoma. On the day before surgery and while on no bronchodilator medication, all subjects performed a progressive histamine inhalation test according to the method of Cockcroft *et al.* The inhalation concentration-response curve was terminated when the FEV<sub>1</sub> had fallen by 20% from resting levels or an inhaled concentration of 16 mg/ml had been reached. The PC<sub>20</sub> was calculated as that concentration of histamine which produced the 20% fall in FEV<sub>1</sub>.

Following surgical removal of the lung, portions of segmental or subsegmental airways were dissected free of lung parenchyma and placed in Krebs-Henseleit solution aerated with 95% O<sub>2</sub> and 5% CO<sub>2</sub>. The airways segments were then cut into spirals, placed in organ baths maintained at 37°C and attached to isometric transducers under an initial tension of 2 g. Changes in tension resulting from the addition of cumulative concentrations of histamine were recorded on a Beckman polygraph. Responses to histamine were expressed as a percentage of the maximum response and the EC<sub>50</sub> calculated. Each piece of bronchial tissue

Ovenhandlers also had a greater prevalence of increased bronchial reactivity ( $PD_{50} < 30 \mu\text{moles}$ ) (56%) than doughmakers (29%) and positive skin tests to wheat (44% vs. 0%,  $p < 0.005$ ). The frequencies for general bakers were intermediate (41% and 17% respectively, NS).

This study demonstrates that bakers have evidence of allergic respiratory disease that is related to their occupational exposure to cereal antigens.

## ROLE OF FOOD ADDITIVES (SODIUM METABISULPHITE AND SALICYLATES) IN CHRONIC CHILDHOOD ASTHMA

S. J. TOWNS AND C. M. MELLIS

*Department of Respiratory Medicine, Royal Alexandra Hospital for Children, Camperdown, NSW*

We have studied the role of two commonly ingested food additives/chemicals, the preservative sodium metabisulphite (MBS) and aspirin (ASA), in 29 children with moderate-severe childhood asthma. All 29 were challenged, single blind, in the pulmonary function laboratory with MBS (capsule form and solution), ASA and placebo. For one week prior to the challenge, and during the challenge period, all 29 were prescribed to full elimination diet. Following the challenges, positive responders to MBS were placed on a diet which excluded MBS containing foods. ASA positive patients were prescribed a diet excluding natural salicylates and advised to avoid aspirin containing medications. After three months on these restricted diets the children were reassessed to determine any therapeutic response.

Sixty six percent (19/29) had a positive immediate challenge ( $> 20\%$  fall in FEV<sub>1</sub>) to metabisulphite and 21% (6/29) had a positive immediate challenge to aspirin. After three months on the restricted diet, 4/19 children on MBS-free diet and 1/6 on salicylate-free diet had objective signs of improvement; namely, a reduction in either steroid or bronchodilator therapy. However, compliance with the diet during these three months was poor, particularly with the aspirin positive children.

We have demonstrated that two commonly ingested chemicals can provoke bronchospasm in asthmatic children. However, elimination of these substances from the diet is difficult and does not, in general, improve the child's asthma.

## THE EFFECT OF PASSIVE CIGARETTE SMOKING ON ASTHMATIC PATIENTS

ALVIN J. JING AND A. B. X. BRESLIN

*Chest Unit, Concord Hospital, Sydney, NSW*

The aim of this study was to examine the effect of passive inhalation of cigarette smoke on airways function in asthmatic patients. Six subjects with bronchial asthma and a history of chest tightness on passive exposure to cigarette smoke were studied. The subjects had well-controlled, mild to moderate asthma. They abstained from beta-2 agonists and inhaled corticosteroids for at least six hours prior to the provocation test, from oral theophylline for 12 hours, from slow release theophylline and sodium cromoglycate for 24 hours and from antihistamines for 48 hours prior to study days. On the first day, baseline FEV<sub>1</sub>,

FVC, MMEFR and peak flow rate readings were undertaken and the patient then sat in a seven cubic metre room for 60 minutes during which time a mechanical device linked to a rheostat was run but no cigarette smoke was produced. Lung function measurements were repeated at 15, 30, 45 and 60 minutes in the room and thereafter every 15 minutes for two hours. On the second day, the same lung function parameters were measured and the patient spent 60 minutes in the same room with the mechanical device producing smoke from cigarettes containing 16 mg of tar and 1.6 mg of nicotine per cigarette at the rate of approximately 100 mls of smoke every two minutes. Carbon monoxide levels were taken in the room after 30 and 60 minutes and pre-exposure and post-exposure venous blood samples were taken and changes in carboxyhemoglobin determined. For the purposes of this study, falls of 20% or more in FEV<sub>1</sub>, FVC and PFR, and 30% in MMEFR, over baseline levels were considered significant.

The concentration of smoke achieved for each individual subject was in the same range of 20-25 parts per million of carbon monoxide, and all subjects had similar rises in carboxyhemoglobin,  $0.5 \pm 0.14\%$ . Chest tightness described as asthma was produced in all six subjects and was described as an average asthmatic attack; the sensation of chest tightness commenced within 15 minutes of smoke exposure and continued for up to one hour post-challenge. These symptoms did not occur on the non-smoke inhalation study day. There were no significant changes in the pulmonary function parameters measured in any of the subjects when compared with baseline values. The largest fall in FEV<sub>1</sub> was 12.55% in one subject, and FEV<sub>1</sub> in this subject did not return to pre-challenge levels for one hour after exposure. Another subject showed a 26.8% fall in MMEFR which also lasted for one hour post-challenge.

Thus, passive exposure to cigarette smoke in these subjects produced marked symptoms described as usual asthma but not significant objective evidence of airways obstruction.

## ASSESSMENT OF BREATHLESSNESS IN ASTHMA

A. NANA, J. G. W. BURDON AND M. C. F. PAIN

*Department of Thoracic Medicine, Royal Melbourne Hospital, Vic*

We report the early results of a study conducted to gain some understanding of the variability of breathlessness in asthma. Using diary cards 21 asthmatic outpatients recorded their symptoms of breathlessness, using a category scaling technique (range; 0 = no breathlessness, 10 = maximum breathlessness), and the severity of their airflow obstruction, assessed by peak expiratory flow rate (PEFR) measurement (Wright's mini-peak flow meter), twice daily (morning and evening) for two weeks.

The results showed that breathlessness increased as PEFR decreased in 17 (81%) patients, but these indices were seemingly unrelated in four others. Despite a close linear relationship in most subjects (mean  $r = 0.74 \pm 0.15$  SD;  $p < 0.001$ ) there was considerable variation in the severity of breathlessness for any particular degree of airflow obstruction (mean intercept on sensory axis  $= 6.3 \pm 4.6$  SD). However the increase in breathlessness with increasing airflow obstruction showed little variation (mean slope  $0.01 \pm 0.01$  SD). The variability in breathlessness in asthma is likely to have many components. In this study we were able to show: (1) that for any given reduction in PEFR, patients with airflow obstruction throughout the study period (mean PEFR  $< 80\%$  predicted) were less breathless than



5

2023379538

Romer, J., Hermann, H. "Significance of Tobacco Smoking for Asthma and Rhinitis" Ugeskr Laeger 145(13): 1025-1027, 1983.

ABSTRACT: Forty-one patients with asthmatic and/or rhinitis and 41 controls of the same age and sex distribution were interviewed about the influence of smoking on health and about their attitude towards the prohibition of smoking in public places.

The study shows that 50% of the asthmatic patients and 36% of the patients with rhinitis develop, at least occasionally, attacks when exposed to smoking.

An increased tendency to coughs and colds was present in both control and patient groups. The numbers are too small to be conclusive. No tendency to an increased incidence of sinusitis [sic] or otitis was observed.

The study points out a significant difference between the patient group and the control group's social engagements, because the allergic patients, to a certain extent, stay away from meetings where smoking occurs.

There are fewer smokers among the allergic patients than among the controls, but the difference is not significant.

Finally, the study shows, in both the patient group and the control group, such a strong dislike of enforced passive smoking that a ban on smoking in public places should be seriously considered, with the provision of special smoking rooms.

2023379539

**UNEDITED TRANSLATION  
PLEASE CHECK ACCURACY**

**NOTE: THIS IS NOT  
CERTIFIED TRANSLATION**

**SIGNIFICANCE OF TOBACCO SMOKING FOR ASTHMA AND RHINITIS**

**by**

**J. Rømer and H. Hermann**

**from**

**Ugeskr Laeger 145(13), 1025-1027 (1983)**

**Translation from Danish**

**IETS/mlb**

**16311**

**2023373540**

# SIGNIFICANCE OF TOBACCO SMOKING FOR ASTHMA AND RHINITIS

by

J. Römer and H. Hermann

## ABSTRACT:

Forty-one patients with asthmatic and/or rhinitis and 41 controls of the same age and sex distribution were interviewed about the influence of smoking on health and about their attitude towards the prohibition of smoking in public places.

The study shows that 50 % of the asthmatic patients and 34 % of the patients with rhinitis develop, at least occasionally, attacks when exposed to smoking.

An increased tendency to coughs and colds was present in both control and patient groups. The numbers are too small to be conclusive. No tendency to an increased incidence of sinusitis or otitis was observed.

The study points out a significant difference between the patient group and the control group's social engagements, because the allergic patients, to a certain extent, stay away from meetings where smoking occurs.

There are fewer smokers among the allergic patients than among the controls, but the difference is not significant.

Finally, the study shows, in both the patient group and the control group, such a strong dislike of enforced passive smoking that a ban on smoking in public places should be seriously considered, with the provision of special smoking rooms.

Tobacco smoke is an irritant of such intensity that it can be suspected as being of significance for patients with asthma and/or rhinitis. The present study has the purpose of elucidating whether patients with asthma or rhinitis show an increased tendency to develop upper respiratory tract infections, otitis media and inflammation of the sinuses or a tendency toward exacerbation of the underlying disease, namely, asthma or rhinitis, as a consequence of active or passive smoking.

The investigation was intended to elucidate whether such tendencies implied social withdrawal.

2023379541

An attempt was also made to determine the attitude of the patient group and of the control group toward passive smoking.

#### Personal Investigations

##### Materials and Methods

The investigation included all patients 16 years old and older (= recorded independently by the health insurance organization) seen in the practice of one of the authors (JR) because of asthma or rhinitis during the course of one year (June 13, 1977 to June 12, 1978), whether or not allergy was found by the allergological investigation, and whether or not such examination was performed.

The group of patients with asthma or hay fever included a total of 66 subjects. Patients who dropped out spontaneously or changed physicians before the investigation began, patients under the age of 16 years (= not registered by the health insurance organization), and patients who did not cooperate adequately, i.e., a total of 23 patients, as well as two persons who at the time of the review of the diagnosis did not know that they should have registered, were eliminated. Forty-one persons remained in the investigation. Their distribution is shown in Table 1.

##### Definitions

Bronchial asthma: attacks of dyspnea of expiratory type.

Allergic rhinitis: attacks of sneezing and running nose without signs of infection and possibly with concomitant conjunctivitis.

Table 1. Patients.

	Allergy		Total
	Demonstrated	Not demon- strated	
Pure asthma	1	4 (2)	5
Pure rhinitis	12	11 (6)	23
Asthma and rhinitis	10	3 (2)	13
	23	18 (10)	41

Allergological examination: at least anamnesis, skin test and RAST [radioallergosorbent test] performed at a specialized department or by a specialist.

The control group was chosen on the basis of a health insurance list to match the patients as to age and sex. Persons with known or suspected allergy are excluded as controls and are replaced by new ones.

A questionnaire was sent to all patients and controls, which was the same for all persons aside from a simple question (concerning asthma and rhinitis). The answers were incomplete in 19 cases (11 patients and 8 controls). One of the authors (JR) complemented the investigation with interviews over the telephone. The questions were not enlarged upon in the telephone interview, but the same wording was used as in the questionnaire. The  $\chi^2$  test was used as the statistical test. A single exception will appear from the text.

2023379543

### Survey of Attitudes

The following questions were asked:

"Should tobacco smoking in public places be allowed without regard to others?"

"Should tobacco smoking in public spaces be restricted to certain rooms and be prohibited in all other rooms?"

If you did not answer with "yes" to one of the two questions above, please answer the following question:

"Should a patient with lung disease or hay fever be able to refuse to tolerate smoking at meetings?"

"If you express your desire to have a meeting without smoking, should it happen?"

- 1) If one individual requests it?
- 2) If the majority are for it?
- 3) Other possibilities?

Five groups are identified on the basis of the answers:

- 1) Does not desire any intervention whatsoever
- 2) Agrees with the ban, if the majority want it
- 3) Agrees with the ban, if a single patient wants it
- 4) Agrees with the ban, if a single -- even healthy -- person wants it
- 5) Would like to see smoking restricted to separate smoking rooms and banned in all other places.

### Results

Fourteen of the 41 patients and 21/41 controls gave positive answers to the question "Do you smoke yourself?". Consequently, there are fewer smokers among the patients, but the difference is not significant.

Ex-smokers who do not smoke currently were asked the question: "Did you stop smoking because of the disease/any disease?" Five of 11 patients and 0/8 controls said yes. The figures show that patients tend to quit smoking because of the disease.

The smokers were asked the question "Have you ever felt inconvenienced by your own smoking?" Six of the 14 patients and 8/21 controls felt inconvenienced by their own smoking.

All persons were asked the question "Has tobacco smoke ever inconvenienced you?" Thirty-seven of the 41 patients and 27/41 controls answered with a yes, i.e., there were significantly more patients than controls among those who said yes (Fisher's exact test:  $p = 0.0087$ ).

In answering the question: "Have you observed any increased tendency to develop asthma, rhinitis, attacks of cough without asthma, sinusitis, otitis media or colds after having been exposed to tobacco smoke?" 13/36 of the rhinitis patients (36%) indicated increased tendency to develop rhinitis and 9/18 of the asthma patients (50%) indicated a correspondingly increased tendency to asthma, or a total of 19 of the 41 patients (46%), because there was an overlap between the two groups, as is indicated in Table 1. Hardly any patients indicated increased tendency to develop sinusitis and otitis media (Table 2).

Both the patient group and the control group show a certain, not significantly different, tendency to develop attacks of cough and colds after exposure to tobacco smoke.

2023379545



Table 2. Answer to the question: "Have you observed increased tendency to the following diseases after having been exposed to tobacco smoke?"

	Number of positive replies	
	Patients	Controls
Attacks of cough	14	9
Sinusitis	1	0
Otitis media	0	0
Colds	8	5
Total, at least one of these	17	11
Total, including asthma or hay fever	24	-

#### Social Consequences

Four patients and three control persons, or less than 10% in both groups, believed they had withdrawn because of exposure to tobacco smoke.

Ten of the asthma/rhinitis patients (24%) said that they were forced to skip meetings where participants smoked -- in response to the question "Can the smoking of other people cause you to stay away from meetings and events?" Only five patients said that they were forced to do so regardless of whether or not they were having asthma/rhinitis symptoms. Three control persons felt forced to stay away (significant difference,  $p = 0.04$ ).

The replies obtained in connection with the attitude investigation are shown in Figure 1. 36/41 patients and 32/41 controls advocate either a total ban on smoking in public places, or when only one person present wishes it. There is no difference in the attitudes of the smokers and nonsmokers, either in the patient group or in the control group.

The numbers are small, but show a widespread attitude against forced passive smoking.

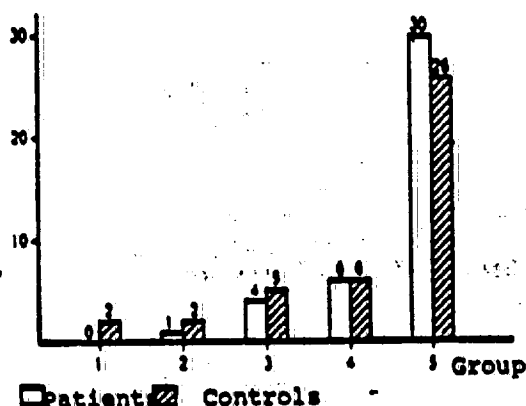


Fig. 1. Attitudes toward smoking in public places.

- Group 1: wishes no intervention whatsoever
- Group 2: wishes ban if the majority are for it
- Group 3: wishes ban if a single patient wishes it
- Group 4: wishes ban if a single, healthy person wishes it
- Group 5: wishes smoking banned and restricted to separate smoking room.

The material is too small for a further breakdown of the patient group to a group which has confirmed allergy and a group in which the tests did not reveal allergy.

#### Discussion

The questionnaire survey shows that 1/3 of the patients with rhinitis and 1/2 of the patients with asthma have increased tendency to attacks of the underlying disease during exposure to tobacco smoke.

The questionnaire survey also seems to show an increased tendency to attacks of cough and common cold after exposure to tobacco smoke.

but the increase is not significant statistically, whereas sinusitis and otitis media were not found as a consequence of tobacco smoking.

The survey shows that tobacco smoking means that certain patients with asthma/rhinitis may feel socially handicapped, at least during the season when the disease flares up.

The small numbers involved in the investigation mean, of course, that the conclusions must be taken with certain reservations as far as the social consequences are concerned. The fact that the persons interviewed knew the authors' personal attitude toward tobacco smoking from the ban on smoking in their waiting room, among other things, can have been of significance in the study of the attitudes.

There are no data to show whether the composition of the population seen in the physician's office differs from the average population. The office is located in an area in the township of Arhus which was selected as an experimental region in other respects, because it is close to the township average.

However, there is reason to believe that the average age was lower than the population average.

The survey also shows that the attitude toward forced passive smoking justifies consideration by the authorities.

White and Froeb [1] concluded from an investigation of 2,100 persons that long-term exposure to tobacco smoke in the working environment (long-term passive smoking = involuntary inhalation of tobacco smoke by nonsmokers) significantly reduced the forced expiratory flow-rate (FEF) and the forced expiratory volume in one second ( $FEV_1$ ), and compared passive smokers with light smokers in this respect.

O'Connell and Logan [2] found that exposure to tobacco smoke significantly aggravated the symptoms in 10% of 400 asthmatic children, and that daily exposure to polluted air (smoking by parents) aggravated the symptoms at least occasionally in 67%.

Based on an investigation of the effects of tobacco smoke in 32 healthy test subjects in a three-hour experiment, Hugod et al. [3] published some unfortunately oft-cited opinions on the harmlessness of long-term passive smoking, opinions which the investigation do not appear to support, but which unfortunately are often mentioned when smokers want to compound their conscience with regard to passive smokers.

Hugod since mentioned in a review article [4] that besides inconveniencing 80% of all nonsmokers, tobacco smoking also has a direct harmful effect on certain groups of patients, including those with asthma, but he did not mention patients with rhinitis. Thus it seems that allergy to tobacco rather than the irritating effect of tobacco smoke is referred to.

It was pointed out by Korsgaard [5] that tobacco consumption exceeding 9 units per day means almost a doubling of the suspended dust concentration in rooms compared with rooms in which tobacco is not smoked daily, but also stressed that there is great controversy worldwide concerning the suspended dust concentrations which cause changes in the status of patients with lung and heart diseases. In view of the fact that tobacco smoking in public places has been banned in 31 states of the United States [6] as well as in Finland and France, the [Danish] parliament must discuss a similar ban without delay. If one wishes to smoke, it is a private

2023379519

matter, but where to smoke is a social issue. 5.2% of the population of Denmark have/had asthma, and 9.4% have/had allergic rhinitis, so that the social aspects are of significance for a large segment of the population [7,8].

Finally, it should also be recommended that an effect does not necessarily have to be harmful to be undesired. Healthy persons also feel inconvenienced without necessarily having social consequences.

Support was granted by Danmarks Asthma-Allergibunds forskningsfond  
[Research Foundation of the Danish Asthma and Allergy Association].

#### REFERENCES

- 1) White JR, Froeb HF. Small-airways dysfunction in nonsmokers chronically exposed to tobacco smoke. *N Engl J Med* 1980; 302: 720-3.
- 2) O'Connell EJ, Logan OB. Parental smoking in childhood asthma. *Ann Allergy* 1974; 32: 142-5.
- 3) Hugod C, Hawkins L, Astrup P. Passivrygning - Eksposition for gasfase- og partikelfasekomponenter i cigarettrøg. *Ugeskr Læger* 1978; 140: 2707-11.
- 4) Hugod C. Passiv rygning. *Ugeskr Læger* 1981; 143: 2181-4.
- 5) Korsgaard J. Indeklimaet i etageboliger. Rapport fra Hygiejnisk institut, Aarhus universitet, og lungeklinikken, Århus kommunehospital, 1981; kap. XI: Svævestøv.
- 6) Egmose T, Heuser A. Håndbog for ikke-rygere. København: Fædli's forlag, 1977: 72.
- 7) Pedersen PA, Weeke EP. Asthma in Danish general practice. *Allergy* 1981; 36: 175-81.
- 8) Pedersen PA, Weeke EP. Allergic rhinitis in Danish general practice. *Allergy* (i trykken).

**2023379551**

Knight, A., Breslin, A.B.X. "Passive cigarette smoking and patients with asthma" Med J Aust 142: 194-195, 1985.

ABSTRACT: A study of the effect of passive smoking on patients with asthma is presented. Six patients were exposed for one hour to the air in a room in which tobacco smoke was produced mechanically over that period. The effects on symptoms, lung function and airways sensitivity to inhaled histamine were then measured and compared with the same patient's responses during a control day when they inhaled smoke-free air. All six patients developed chest tightness and symptoms similar to an attack of asthma. The findings of respiratory and sensitivity tests suggest: (i) that passive smoking may trigger asthma attacks in subjects who suffer from asthma and (ii) that the airways of such subjects show increased histamine reactivity four hours after the passive smoke exposure.

2023379552

15. Russell MAH. Nicotine intake and its regulation. *J Psychosom Res* 1980; 24: 253-264.
16. Ashton H, Stepney R, Thompson JW. Self-titration by cigarette smokers. *Br Med J* 1979; 2: 357-360.
17. Gibson J, Gallagher H, Johansen A, Webster L. Lung function in an Australian population: spirometric performance and cigarette-smoking habits. *Med J Aust* 1979; 1: 354-358.
18. Brockway BS. Chemical validation of self-reported smoking rates. *Behav Res Ther* 1980; 6: 12.
19. Vogt TM, Selvin S, Billings JH. Smoking cessation program: baseline carbon monoxide and serum thiocyanate levels as predictors of outcome. *Am J Public Health* 1979; 69: 1156-1159.
20. Research Committee of the British Thoracic Society. Comparison of four methods of smoking withdrawal in patients with smoking related diseases. *Br Med J* 1983; 286: 595-597.
21. Hunt WA, Matarazzo JD. Habit mechanisms in smoking. In: Hunt WA, ed. Learning mechanisms in smoking. Chicago: Aldine, 1970: 65-106.
22. Hunt WA, Barnett LW, Branch LG. Relapse rates in addiction programs. *J Clin Psychol* 1971; 27: 455-456.
23. Kuller L, Meilahn E, Townsend M, Weinberg G. Control of cigarette smoking from a medical perspective. *Ann Rev Public Health* 1982; 3: 153-178.

(Received June 6; accepted August 13, 1984)

(for editorial comment, see page 176)

## Passive cigarette smoking and patients with asthma

Anne Knight and Antony B.X. Breslin

**ABSTRACT:** A study of the effect of passive smoking on patients with asthma is presented. Six patients were exposed for one hour to the air in a room in which tobacco smoke was produced mechanically over that period. The effects on symptoms, lung function and airways sensitivity to inhaled histamine were then measured and compared with the same patient's responses during a control day when they inhaled smoke-

free air. All six patients developed chest tightness, and symptoms similar to an attack of asthma. The findings of respiratory and sensitivity tests suggest: (i) that passive smoking may trigger asthma attacks in subjects who suffer from asthma and (ii) that the airways of such subjects show increased histamine reactivity four hours after the passive smoke exposure.

(Med J Aust 1985; 142: 194-195)

**PATIENTS WITH asthma** who do not smoke commonly complain of "chest tightness" or wheezing as well as upper-respiratory tract symptoms when they are exposed to other people's cigarette smoke. This subjective response has been documented,<sup>1,2</sup> but objective studies of changes in lung function give conflicting results.<sup>3,4</sup>

A lack of effect of active cigarette smoking on the bronchial sensitivity to histamine and methacholine immediately after smoking a cigarette has been demonstrated.<sup>5</sup> Young asymptomatic smokers have been shown to be no more responsive to inhaled histamine than are non-smokers.<sup>6</sup> However, the effect of passive smoking on bronchial reactivity has not been studied in patients with asthma.

The aim of this study was to investigate the acute respiratory response in patients with mild to moderate asthma to passive cigarette smoking and to assess whether passive smoke inhalation alters bronchial sensitivity to inhaled histamine.

### Methods

Six subjects with mild to moderate asthma who were non-smokers were studied on an outpatient basis over two days. They were exposed to the air of a provocation room in which smoke was produced mechanically from one cigarette after another, continuously, over one hour. (Details of procedures and equipment used may be obtained from the writers on request.) The two-day study was organized as follows:

#### Day 1

##### Baseline lung function

Respiratory Unit, Concord Hospital, Concord, NSW 2139.  
Anne Knight, MB BS, Medical Student.  
Antony B.X. Breslin, MB BS, FRACP, Senior Specialist in Charge.  
Reprints: Dr A.B.X. Breslin.

#### Histamine inhalation test (HIT)

Sixty minutes in room, cigarette not lit.  
Repeat HIT four hours after leaving the room

#### Day 2

##### Baseline lung function

##### HIT

Sixty minutes in room; cigarette lit  
Repeat HIT four hours after leaving room

The parameters of lung function chosen were the forced expiratory volume in one second (FEV<sub>1</sub>), the vital capacity (VC) and the maximum mid-expiratory flow rate (MMEFR) with the same Vitalograph spirometer used for all measurements, and the peak expiratory flow rate (PEFR) measured by means of a Wright Peak Flow Meter. Measurements were taken at 15-minute intervals while in the provocation room, and afterwards until the readings had returned to baseline.

Each patient underwent four HITs during the study, and for each test the provocative concentration of histamine which produced a 20% fall in FEV<sub>1</sub> from a baseline value (PC<sub>20</sub>) was calculated.

### Results

Patient profiles are shown in Table 1. All six patients experienced some symptoms as a result of the passive smoking, eye irritation being the most common complaint. The four patients who gave a positive history of asthma attacks induced by passive smoking experienced "chest tightness" — of a mild degree for subjects 1 and 2 and of a moderate degree for subject 4 — and/or wheezing (subjects 4 and 5). Rhonchi (which had not been heard before the challenge) were heard on auscultation at the end of the exposure to smoke-contaminated air in subjects 4 and 5.

The changes in FEV<sub>1</sub> (expressed as percentage change from the baseline) on both days are presented in Table 2. All

2023379553



six subjects showed falls in FEV<sub>1</sub> on the challenge day, the mean maximum fall being 11% compared with a mean maximum rise on the control day of 4.6%. These changes were statistically significant, according to a two-tailed paired

TABLE 1: Patient profiles

	Subject number					
	1	2	3	4	5	6
Age (years)	23	23	24	22	22	39
Sex	M	M	M	F	M	F
Number of positive skin prick tests to 23 common allergens	5	2	2	3	10	3
IgE level (u/mL)	140	43	1220	330	1140	310
History of "chest tightness" or wheezing in response to passive smoking	Yes	Yes	No	Yes	Yes	No

TABLE 2: Maximum variations of FEV<sub>1</sub> from baseline

Subject Number	Control day	Challenge day	Significance
1	+1.3%	-8.5%	$P > 0.05$
2	+3.3%	-5.0%	$P > 0.05$
3	+5.1%	-1.7%	$P > 0.05$
4	+5.8%	-15.1%	$P < 0.001$
5	+2.8%	-26.9%	$P < 0.055$
6	+9.5%	-8.7%	$P < 0.001$

TABLE 3: PC<sub>20</sub> values before entering and four hours after leaving the provocation room\*

	Subject number					
	1	2	3	4	5	6
Control day						
PC <sub>20</sub> before	4.39	6.96	1.60	0.86	0.39	0.74
PC <sub>20</sub> after	4.44	6.96	2.85	0.77	0.47	0.66
Challenge day						
PC <sub>20</sub> before	4.59	7.21	0.92	0.90	0.22	1.00
PC <sub>20</sub> after	1.07	6.96	0.24	0.64	0.09	0.53
PC <sub>20</sub> before/PC <sub>20</sub> after						
Control day	0.99	1.00	0.57	1.12	0.83	1.12
Challenge day	4.29	1.04	3.83	1.41	2.44	1.89

\*PC<sub>20</sub> = provocative concentration of histamine (g/L) that produces a 20% fall in FEV<sub>1</sub> from a baseline value.

## References

1. Weber A, Fisher T, Grandjean E. Passive smoking in experimental and field conditions. *Environ Res* 1979; 20: 205-216.
2. Speer F. Tobacco and the non-smoker. A study of subjective symptoms. *Arch Environ Health* 1968; 16: 443-446.
3. Shephard RJ, Collins R, Silverman F. "Passive" exposure of asthmatic subjects to cigarette smoke. *Environ Res* 1979; 20: 392-402.
4. Dahms TE, Bolin JF, Slavin RG. Passive smoking: effects on bronchial asthma. *Chest* 1981; 80: 530-534.

t-test, in subjects 4, 5 and 6; subjects 1, 2 and 3 showed similar, though not statistically significant, changes. Similar trends were seen in VC, MMEFR and PEFR.

The results of the HITs are shown in Table 3. There was a trend for the PC<sub>20</sub> to fall after exposure to smoke to an extent which was not found on the control day. All but subject 2 had their lowest PC<sub>20</sub> at four hours after smoke provocation. The changes in PC<sub>20</sub> produced by passive smoking were statistically significant for the group, and indicate an increased airway irritability induced by passive smoking which was still detectable at four hours after cessation of exposure to ambient smoke.

## Discussion

Variable deteriorations in lung function parameters as a result of passive exposure to ambient cigarette smoke were found in all the subjects in our study. These deteriorations did not correlate with chest symptoms. In comparison with our findings, Dahms et al. observed a mean change of 21.4% in FEV<sub>1</sub> in 10 asthmatic subjects exposed passively to cigarette smoke.<sup>4</sup>

As a control day was included in the protocol, it is unlikely that the significant trend for the PC<sub>20</sub> to decrease which we observed at four hours after smoke exposure was due to diurnal variation or to variability in the test.

A four-hour interval between leaving the provocation room and performing the post-challenge HIT was chosen because animal studies have shown that neutrophil infiltration in response to airborne antigens is accompanied by an increase in histamine reactivity at four hours after a challenge.<sup>7</sup>

Thus our findings suggest that passive smoke inhalation may produce asthma attacks in subjects who suffer from asthma and may lead to increased bronchial reactivity to histamine for a time after such inhalation. Thus, the airways may be primed to react more vigorously to other triggers (for example, emotion, cold air, exercise) thereby initiating an attack which would not otherwise have occurred. This has obvious social implications for subjects with asthma who are frequently exposed to other people's cigarette smoke.

5. McIntyre EL, Ruffin RE, Alpers JH. Lack of short-term effects of cigarette smoking on bronchial sensitivity to histamine and methacholine. *Eur J Respir Dis* 1982; 63: 535-542.
6. Cockcroft DW, Borechod BA, Murdock KY. Bronchial response to inhaled histamine in asymptomatic young smokers. *Eur J Respir Dis* 1983; 64: 207-211.
7. Irvin CG, Henson PM, Berend N. Acute effects of airways inflammation on airway function and reactivity. *Fed Am Soc Exp Biol [Fed Proc]* 1982; 41: 1358.

(Received April 26; accepted September 21, 1984)

2023379554

7

**2023379555**

Wiedemann, H.P., Mahler, D.A., Loke, J., Virgulto, J.A., Snyder, P., Matthay, R.A. "Acute Effects of Passive Smoking on Lung Function and Airway Reactivity in Asthmatic Subjects" Chest 89: 180-185, 1986.

ABSTRACT. We studied the acute effects of one hour of passive cigarette smoking on the lung function and airway reactivity of nine young adult asthmatic volunteers. At the time of this study, the subjects were asymptomatic and had normal or nearly normal lung function. Passive smoking produced no change in expiratory flow rates. However, there was a small decrease in nonspecific bronchial reactivity, as assessed by methacholine inhalation challenge testing ( $p=0.022$ ). Pharmacologically active substances present in cigarette smoke, such as nicotine, may explain the observed change in airway reactivity. Although the finding of decreased airway reactivity might suggest that passive smoking produces a "protective" effect on the underlying asthma, the observed change in reactivity was slight and of uncertain clinical significance. We conclude that passive smoking presents no acute respiratory risk to young asymptomatic asthmatic patients.

2023379556

# Acute Effects of Passive Smoking on Lung Function and Airway Reactivity in Asthmatic Subjects\*

Herbert P. Wiedemann, M.D.;† Donald A. Mahler, M.D., F.C.C.P.;  
Jacob Loke, M.D.; James A. Virgulto, C.C.E.; Peter Snyder, R.R.T.; and  
Richard A. Matthay, M.D., F.C.C.P.

We studied the acute effects of one hour of passive cigarette smoking on the lung function and airway reactivity of nine young adult asthmatic volunteers. At the time of this study, the subjects were asymptomatic and had normal or nearly normal lung function. Passive smoking produced no change in expiratory flow rates. However, there was a small decrease in nonspecific bronchial reactivity, as assessed by methacholine inhalation challenge testing ( $p = 0.022$ ). Pharmacologically active substances present in cigarette smoke,

such as nicotine, may explain the observed change in airway reactivity. Although the finding of decreased airway reactivity might suggest that passive smoking produces a "protective" effect on the underlying asthma, the observed change in reactivity was slight and of uncertain clinical significance. We conclude that passive smoking presents no acute respiratory risk to young asymptomatic asthmatic patients.

Nonsmokers are frequently exposed to tobacco smoke in indoor environments. The potential health risks of such involuntary, or passive, smoking is a topic of intense interest.<sup>1,2</sup> Current evidence suggests that passive smoking acutely lowers the angina threshold<sup>3</sup> and that chronic passive smoking may lead to small airways dysfunction<sup>4</sup> or lung cancer.<sup>5</sup> There is a paucity of data on whether asthmatics may be at special respiratory risk from passive smoking.

Asthma is characterized by hyperreactivity of the airways, such that a wide variety of different stimuli may cause bronchospasm and reduced airflow. Even if lung function tests are normal, bronchial hyperreac-

important since many studies have shown a correlation of airway reactivity with the clinical severity of asthma as determined by symptom scores, medication requirements, or dose of specific allergen required to produce airflow obstruction.<sup>6-10</sup>

Two previous studies which examined the acute effects of passive smoking on lung function in asthmatics report conflicting results.<sup>11,12</sup> Furthermore, there is no published information concerning the effect of passive smoking on nonspecific airway responsiveness in asthmatics. Therefore, we investigated the effect of acute passive smoking on both lung function and airway reactivity in a group of young stable asthmatic patients.

For editorial comment see page 161

tivity can be detected by bronchoprovocation challenge testing with inhaled agents such as histamine or methacholine.<sup>13</sup> In addition, bronchoprovocation testing may be useful for detecting changes in airway reactivity that occur in response to therapeutic interventions or environmental exposures. For example, such studies have demonstrated temporary increases in bronchial responsiveness following viral infections,<sup>14</sup> and antigen inhalation,<sup>15</sup> as well as exposure to ozone<sup>16</sup> and nitrogen dioxide.<sup>17</sup> Changes in nonspecific bronchial responsiveness may be clinically

## SUBJECTS AND METHODS

Nine asthmatic individuals ranging in age from 19 to 30 years were studied. Five subjects were males, and four were females. Subjects were selected from 11 consecutive respondents to an advertisement announcing the study. The diagnosis of asthma was made previously by the individual's physician. Respondents were included only if they were currently clinically stable and off oral asthma medications. Four individuals intermittently using inhaled bronchodilators at the time of the study were included. No subject with an upper respiratory infection within the preceding eight weeks was studied. Although the subjects were asymptomatic at the time of this study, five had required hospitalization for asthma in the past. However, no subject had been hospitalized for asthma within the preceding year. All individuals were nonsmokers. Individuals were not selected based upon a history of how they reacted in the presence of tobacco smoke. However, six of the subjects indicated that exposure to cigarette smoke "bothered" their asthma.

Subjects were instructed to avoid coffee, cola drinks, chocolate, and exercise for at least six hours before bronchoprovocation testing. No subject was taking vitamin C supplements. Subjects using an inhaled bronchodilator were instructed to withhold use for six to eight hours preceding the test, in accordance with published guidelines.<sup>18</sup> Before participation in the study, subjects signed a

\*From the Pulmonary Section, Department of Medicine, Yale University School of Medicine, New Haven, CT.

†Staff Physician, Pulmonary Department, Head, Section of Respiratory Therapy, Cleveland Clinic Foundation, Cleveland.

This study was supported in part by a grant from the Connecticut Affiliate of the American Lung Association. Presented in part at the American Thoracic Society annual meeting in Kansas City, 1983.

Manuscript received March 11; revision accepted September 3.  
Reprint requests: Dr. Wiedemann, Pulmonary Department, Cleveland Clinic, 9500 Euclid Avenue, Cleveland 44106.

Table 1—Protocol

Day 1	Day 2
I. Baseline studies	I. Before passive smoking
a. Spirometry (FEV <sub>1</sub> , FVC, Vmax50)	a. Venous COHb analysis
b. Methacholine inhalation challenge	b. Spirometry
	II. One hour smoke exposure
	III. After passive smoking
	a. Venous COHb analysis
	b. Spirometry
	c. Methacholine inhalation challenge

consent form approved by the Yale Human Investigation Committee.

The experimental protocol was carried out in each subject on two separate days (Table 1). This design was utilized in order to avoid the need to do two methacholine challenges on the same day.<sup>24</sup> On the first day, baseline spirometry was measured with a pneumotachograph-integrated flow-volume device<sup>25</sup> connected to a Gould 3054 high performance X-Y recorder. The forced vital capacity (FVC), the forced expiratory volume in one second (FEV<sub>1</sub>), and the maximal expiratory flow rate at 50 percent of the vital capacity (Vmax50) were determined. Following this, a methacholine inhalation challenge test was performed. The challenge test was conducted by delivering sequential doses of methacholine in phenol-buffered saline solution (0.05, 0.5, 1.0, 2.0, 5.0, 10.0, 25.0 mg/ml) via mouthpiece with a DeVilbiss No. 45 nebulizer. A noseclip was used. Each dose was delivered during two minutes of normal tidal breathing. The FEV<sub>1</sub> was determined at 0.5 and four minutes after each dose. If at either time there was a 20 percent or greater fall in FEV<sub>1</sub> from the baseline prechallenge value, the test was terminated. If the FEV<sub>1</sub> did not decrease by this amount, then the next dose was delivered. The cumulative dose of methacholine which corresponded to a 20 percent decrease in FEV<sub>1</sub> was determined by linear interpolation of the last two points on the dose-response curve.<sup>26</sup> This "provocative dose" of methacholine which causes a 20 percent decrease in FEV<sub>1</sub> is the PD<sub>20</sub>FEV<sub>1</sub>. A low PD<sub>20</sub>FEV<sub>1</sub> indicates a high degree of non-specific bronchial responsiveness.

On the second experiment day (24 to 48 hours following the first day), subjects returned for spirometry and then a baseline pre-smoke exposure venous blood sample was drawn for carboxyhemoglobin (COHb) analysis. The blood COHb level analysis was performed with a double-wavelength spectrophotometer.<sup>27</sup> The subject then entered a 25 m<sup>3</sup> environmental chamber for exposure to machine-generated cigarette smoke for one hour. Both sidestream and mainstream smoke filled the chamber. The same brand of a leading nonfilter cigarette was used in all experiments. The chamber was maintained at a temperature of about 25°C and the relative humidity was approximately 50 percent. Air turnover in the chamber was adjusted as necessary to maintain a carbon monoxide level in the ambient air of between 40 and 50 ppm. The carbon monoxide level was sampled continuously from an area near the subject. While in the chamber, the subjects were given the option to wear goggles to reduce eye irritation. These goggles did not cover the nose or mouth.

Immediately following one hour of passive smoking, the subject exited from the chamber and a venous blood sample was drawn for COHb analysis. Spirometric testing was performed, followed by a methacholine bronchoprovocation challenge. The chest of each subject was auscultated immediately before and after the passive smoke exposure.

A methacholine challenge test was also administered to 14 individuals (age 18 to 37 years, mean 28 years) who had normal pulmonary function test results and no history of asthma. The purpose was to compare the methacholine responsiveness of this

Table 2—Individual Results of Lung Function and PD<sub>20</sub>FEV<sub>1</sub> in Asthmatic Subjects

Subject	Test	Day 1	Day 2	
			Presmoke	Postsmoke
1.	FEV <sub>1</sub> (L)	3.63	3.55	3.55
	Vmax50 (L/sec)	4.30	4.00	3.90
	FVC (L)	4.53	4.60	4.55
	PD <sub>20</sub> FEV <sub>1</sub> (mg/ml)	.43		.72
2.	FEV <sub>1</sub>	3.05	2.75	2.85
	Vmax50	2.30	2.00	2.10
	FVC	4.80	4.53	4.40
	PD <sub>20</sub> FEV <sub>1</sub>	.027		.070
3.	FEV <sub>1</sub>	3.05	3.10	2.95
	Vmax50	2.95	2.70	2.50
	FVC	4.20	4.37	4.10
	PD <sub>20</sub> FEV <sub>1</sub>	.086		.120
4.	FEV <sub>1</sub>	4.05	4.05	4.08
	Vmax50	3.60	3.40	3.60
	FVC	5.55	5.65	5.63
	PD <sub>20</sub> FEV <sub>1</sub>	.260		.720
5.	FEV <sub>1</sub>	3.30	3.10	3.13
	Vmax50	3.35	2.70	2.90
	FVC	4.45	4.38	4.30
	PD <sub>20</sub> FEV <sub>1</sub>	.675		1.72
6.	FEV <sub>1</sub>	4.10	4.50	4.40
	Vmax50	5.30	5.00	4.60
	FVC	4.73	5.15	5.10
	PD <sub>20</sub> FEV <sub>1</sub>	.34		.21
7.	FEV <sub>1</sub>	4.15	4.33	4.23
	Vmax50	4.80	5.30	5.20
	FVC	5.05	5.20	5.10
	PD <sub>20</sub> FEV <sub>1</sub>	.37		3.45
8.	FEV <sub>1</sub>	2.70	3.05	3.00
	Vmax50	2.60	3.60	3.40
	FVC	3.63	3.75	3.75
	PD <sub>20</sub> FEV <sub>1</sub>	.037		.073
9.	FEV <sub>1</sub>	2.90	2.90	2.90
	Vmax50	2.00	2.40	2.60
	FVC	4.20	4.25	4.15
	PD <sub>20</sub> FEV <sub>1</sub>	.040		.047

"normal" group with that of the study population, which had been selected based upon a prior history of asthma. The normal individuals did not participate in the passive smoking experiment.

Statistical analyses of spirometric values, carboxyhemoglobin levels, and the PD<sub>20</sub>FEV<sub>1</sub> transformed to log units as is customary were performed with the paired Student's *t*-test. The nonparametric signed rank test was used to also evaluate changes in PD<sub>20</sub>FEV<sub>1</sub> assessed without prior transformation to log units.

## RESULTS

Results obtained in individual subjects are shown in Table 2. Mean data and statistical comparisons between groups of paired data are provided in Table 3.

### Symptoms and Signs

Marked eye irritation was a universal finding. Most individuals opted to wear the protective goggles after spending several minutes in the chamber. Three subjects experienced mild, transient, self-limiting cough. Except for eye and nasopharyngeal irritation, the

Table 3—Mean Results of Lung Function, Carboxyhemoglobin Levels, and PD<sub>20</sub>FEV<sub>1</sub>

	Day 1	Day 2	
	Baseline	Presmoke	Postsmoke
FEV <sub>1</sub> (L)	3.43 ± .57	3.48 ± .65	3.45 ± .63
V <sub>max50</sub> (L/sec)	3.46 ± 1.14	3.46 ± 1.14	3.42 ± 1.02
FVC (L)	4.57 ± 0.55	4.65 ± 0.58*	4.56 ± 0.60* *p = 0.01
COHb (%)		1.71 ± 0.89	2.57 ± 1.05 p = 0.001
PD <sub>20</sub> FEV <sub>1</sub> (mg/ml)	0.25 ± 0.22		0.79 ± 1.13 p = 0.043
log PD <sub>20</sub> FEV <sub>1</sub>	-1.92 ± 1.23		-1.21 ± 1.54 p = 0.022

\*Data expressed as mean ± SD.

subjects were comfortable and spent the time in the chamber reading or studying. No subject complained of headache, chest pain, or abdominal pain. No subject had wheezes detectable by auscultation either immediately before or after the period of involuntary smoking.

#### Blood Carboxyhemoglobin Analysis

The pre-exposure venous blood carboxyhemoglobin (COHb) level was  $1.71 \pm 0.89$  percent (mean ± SD). Following passive smoking, the COHb level was  $2.57 \pm 1.05$  ( $p < 0.001$ ). This represents an increase in

the mean COHb level of 0.86. This is in close agreement with the expected increase in COHb content following exposure to 40 to 50 ppm carbon monoxide for 60 minutes.<sup>24,25</sup>

#### Lung Function

Results of baseline lung function on day 1 were normal in four subjects, showed small airways obstruction in another four subjects, and revealed mild airways obstruction (FEV<sub>1</sub> between 65 percent and 80 percent of predicted) in one subject. There was no difference between day 1 baseline lung function and day 2 pre-smoke lung function. Comparison of day 2 presmoke lung function and postsmoke lung function showed no difference in FEV<sub>1</sub> or V<sub>max50</sub>. The FVC showed a small decrease (2 percent) following passive smoking ( $p = 0.01$ ).

#### Airway Reactivity

The baseline PD<sub>20</sub>FEV<sub>1</sub> on day 1 showed that each subject had a high degree of nonspecific bronchial responsiveness compared to a normal population

#### METHACHOLINE RESPONSIVENESS IN NORMALS AND ASTHMATIC SUBJECTS

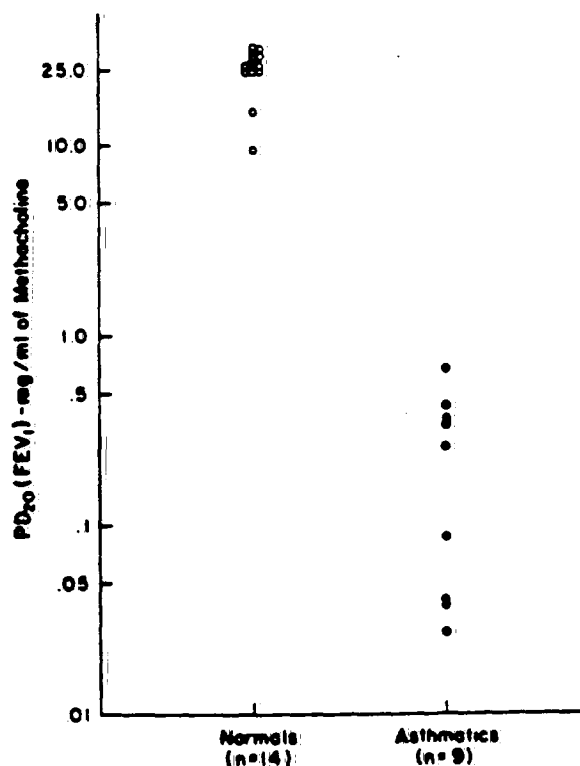


FIGURE 1. The methacholine responsiveness of the study population is compared with individuals who gave no history of asthma. The asthmatic subjects have a very low PD<sub>20</sub>FEV<sub>1</sub>, indicating a high degree of airway reactivity.

#### METHACHOLINE RESPONSIVENESS (PD<sub>20</sub>FEV<sub>1</sub>) BEFORE AND AFTER PASSIVE CIGARETTE SMOKE EXPOSURE

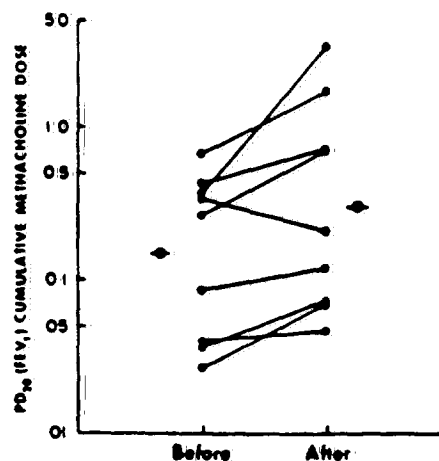


FIGURE 2. This illustrates the methacholine responsiveness in nine stable asthmatics before and after passive smoking. Exposure to cigarette smoke resulted in an increased PD<sub>20</sub>FEV<sub>1</sub>, indicating a decrease in airway reactivity ( $p = 0.022$ ). The mean values are also illustrated (antilog of the mean of the log PD<sub>20</sub>FEV<sub>1</sub> values).

tested in our laboratory (Fig 1). This is to be expected but confirms that our subjects, who were asymptomatic at the time of testing, are asthmatics.

A comparison of baseline  $PD_{20}FEV_1$  on day 1 with postexposure day 2 is provided in Figure 2. Eight of the nine subjects showed an increase in  $PD_{20}FEV_1$ . The mean  $PD_{20}FEV_1$  before smoke was  $25 \pm 22$  mg/ml and after exposure was  $79 \pm 1.13$  mg/ml ( $p = 0.04$ ) while the log  $PD_{20}FEV_1$  increased from  $-1.92$  to  $-1.21$  ( $p = 0.02$ ).

#### DISCUSSION

Involuntary smoking produces unpleasant symptoms in many individuals.<sup>11,12</sup> These subjective complaints may be sufficient cause to regulate smoking in confined public places. However, it remains controversial whether acute passive smoking is associated with important pulmonary physiologic hazards. The present study was designed to investigate whether involuntary smoking presents an acute respiratory risk to asymptomatic asthmatic individuals.

Our data demonstrate that one hour of passive cigarette smoke inhalation by young, clinically stable asthmatics produced no change in maximal expiratory flow rates. Furthermore, passive smoking caused a slight decrease in nonspecific bronchial reactivity assessed via methacholine bronchoprovocation. Our subjects were exposed to a severe simulation of passive smoking, beyond what normally occurs in the majority of social or occupational environments.<sup>13</sup> A carbon monoxide level in the ambient air of 40 to 50 ppm far exceeds the level found in office environments where smoking is permitted and is higher than the peak hourly averages usually found in taverns or nightclubs.<sup>14</sup> Blood carboxyhemoglobin determinations confirmed the degree of passive smoke inhalation by our subjects.

Two previous studies<sup>15,16</sup> investigated the effect of passive smoking on lung function in asthmatics, however, neither evaluated the influence of such involuntary smoking on airway reactivity. Shephard et al<sup>15</sup> studied 14 asthmatic subjects and found that the  $FEV_1$  and  $V_{max50}$  were unchanged after passive smoking. In their study, the intensity of exposure was less (carbon monoxide level in chamber was about 24 ppm), but the duration was longer (two hours). Their subjects were older than ours. Furthermore, the baseline pulmonary function of their subjects demonstrated airflow obstruction ( $FEV_1 = 68 \pm 19$  percent of predicted, range 30 percent to 91 percent) and several of the subjects were receiving oral asthma medications. Additionally, four of their subjects gave a specific history of "exacerbation" with exposure to cigarette smoke; nevertheless, this subgroup also experienced no decrement in pulmonary function. In contrast to our results and those of Shephard et al,<sup>15</sup> Dahms et al<sup>16</sup>

demonstrated a 20 percent decrease in  $FEV_1$  and FVC following passive smoking in ten patients with bronchial asthma. It is difficult to account for the different results based upon experiment design or patient selection, although such factors may have played a role. In Dahms' study, the smoke exposure was less intense (one hour of a calculated carbon dioxide concentration of 15 to 20 ppm; the average increase in COHb level during exposure was 0.40). Their patients were young (age 18 to 26 years), and baseline lung function demonstrated only mild impairment; the mean FVC was 79.2 percent of predicted and the mean  $FEV_1$  was 73.7 percent of predicted. The subjects continued taking medications (except bronchodilators beginning four hours prior to exposure), but the authors did not describe what medications were taken and how many subjects were on medications. However, one-half of their subjects were included because of a history of specific complaints when exposed to cigarette smoke; only the remaining five were recruited at random. In short, our study is in agreement with Shephard et al<sup>15</sup> and acute at variance with Dahms et al<sup>16</sup> regarding the effect of passive smoking on maximal expiratory flow in asthmatics. The present study additionally investigated the effect of passive smoking on bronchial reactivity.

The finding that passive smoking caused a decrease in nonspecific airway responsiveness (increased  $PD_{20}FEV_1$ ) was unexpected. The clinical significance of the change is uncertain, since the magnitude was small. Only one subject had a change in  $PD_{20}FEV_1$  of at least one log dose (tenfold shift), an increment that is considered clinically important.<sup>17</sup> It is not known whether lesser changes in  $PD_{20}FEV_1$  are important. Although our data show that passive smoking caused a small decrease in airway reactivity, the possibility that this could be associated with an amelioration of the underlying asthma cannot be determined from our study.

The reduction in nonspecific airway responsiveness that we observed might have been mediated by pharmacologically active substances present in cigarette smoke. Inhalation of cigarette smoke causes increased plasma levels of the sympathetic neurotransmitter norepinephrine as well as the adrenomedullary hormone epinephrine.<sup>18</sup> It is possible that catecholamines released locally from sympathetic nerve ganglia, or into the circulation from the adrenal glands, may modify airway smooth muscle reactions. Catecholamine release in response to tobacco smoke inhalation is probably mediated by nicotine. Increased blood and urinary nicotine levels are found in people with mild to moderate passive smoking exposures.<sup>19,20</sup> Wallis et al<sup>21</sup> have demonstrated that inhalation of nicotine diminished airway responsiveness to methacholine in baboons who were highly reactive to methacholine; even

though nicotine inhalation had no direct bronchodilator effect on lung function.

Quantification of bronchial responsiveness may be affected by the prechallenge airway caliber.<sup>22,23</sup> This might be due to altered distribution of inhaled aerosol particles, such that a greater portion may deposit on the segmental airways, a site where constriction has a profound effect on the FEV<sub>1</sub>. Furthermore, the exponential relationship between airway diameter and resistance to airflow may mean that an equivalent amount of airway narrowing may cause a much greater decrement in FEV<sub>1</sub> in a patient who started the challenge test with constricted airways. Since the lung function of our subjects was the same prior to each of the two methacholine tests, the influence of baseline airway caliber probably was not important in our results.

The FEV<sub>1</sub> test requires a forced vital capacity maneuver following inspiration to total lung capacity. Full lung inflation can reduce or abolish bronchoconstriction induced by pharmacologic agents in healthy subjects.<sup>9</sup> Thus, detecting slight airway responses to inhaled agents in healthy nonasthmatic subjects requires the use of lung function tests that do not involve inspiration to total lung capacity. In such cases, partial expiratory flow volume curve initiated from end-tidal inspiration, or plethysmographic measurements of airway resistance (SGaw) can be utilized. However, in asthmatics, reduction of bronchomotor tone by lung inflation is minimal or absent, and therefore, the FEV<sub>1</sub> is a useful and reliable test for assessing bronchial reactivity in such patients.<sup>24</sup> Furthermore, SGaw may be influenced by suggestion, whereas FEV<sub>1</sub> generally is not.<sup>24,25</sup> This may be due to vagal pathways causing subtle changes in large airway tone. Eliminating the effect of suggestion is important in this study, where the subject cannot be "blinded" to the presence of cigarette smoke. And finally, the PD<sub>50</sub>FEV<sub>1</sub> shows less day-to-day variability than PD<sub>50</sub>SGaw and may be a better test to use when comparing bronchoprovocation tests performed on different days.<sup>9</sup>

We emphasize that this study did not evaluate several aspects that may be relevant to the "real life" problem of passive smoking by asthmatics. Our investigation evaluated only the immediate effects of a one-hour period of involuntary smoking. We did not test whether delayed effects of an acute exposure may occur. Furthermore, our subjects had virtually normal lung function during the study and the findings might be different for asthmatics exposed to cigarette smoke during an episode of bronchospasm. Not to be overlooked is the possible effect of chronic passive smoking. Chronic cigarette smoking may lead to increased airway reactivity in normal subjects.<sup>26,27</sup> By analogy, chronic involuntary smoking might lead to clinical deterioration in asthmatics. Also, the development or

severity of asthma in children may be influenced by parental smoking.<sup>28</sup> And finally, there may be a subset of asthmatics with a specific allergy to constituents of tobacco smoke.<sup>29</sup> Further work will be required to elucidate whether passive cigarette smoking represents a risk to such individuals. Nevertheless, the current study suggests that passive cigarette smoking presents no acute respiratory risk to young asymptomatic asthmatics.

## References

- 1 Weiss ST, Tager IB, Schenker M, Speizer FE. The health effects of involuntary smoking. *Am Rev Respir Dis* 1983; 128:933-42.
- 2 Lefcoe NM, Ashley MJ, Pederson LL, Keays JJ. The health risks of passive smoking: the growing case for control measures in enclosed environments. *Chest* 1983; 84:90-95.
- 3 Aronow WS. Effect of passive smoking on angina pectoris. *N Engl J Med* 1978; 299:21-24.
- 4 White JR, Froeb HF. Small-airways dysfunction in nonsmokers chronically exposed to tobacco smoke. *N Engl J Med* 1980; 302:720-23.
- 5 Hirayama T. Nonsmoking wives of heavy smokers have a higher risk of lung cancer: a study from Japan. *Br Med J* 1961; 282:183-85.
- 6 Fish JE, Menkes HA. Airway reactivity: role in acute and chronic disease. In: Simmons DH, ed. *Current pulmonology*, vol 5. New York: John Wiley and Sons, 1984:169-99.
- 7 Hargreave FE, Ryan G, Thomson NC, O'Byrne PM, Latimer K, Juniper EF, et al. Bronchial responsiveness to histamine or methacholine in asthma: measurement and clinical significance. *J Allerg Clin Immunol* 1981; 68:347-55.
- 8 Fish JE, Kelly JF. Measurements of responsiveness in bronchoprovocation testing. *J Allerg Clin Immunol* 1979; 64(part 2):592-96.
- 9 Townley RG, Bewtra AK, Nair NM, Brodkey FD, Watt GD, Burke KM. Metacholine inhalation challenge studies. *J Allerg Clin Immunol* 1979; 64(part 2):569-74.
- 10 Hargreave FE, Dolovich J. Nonspecific bronchial responsiveness. *Chest* 1982; 82(suppl):22-23.
- 11 Guidelines for bronchial inhalation challenges with pharmacologic and antigenic agents. *Am Thorac Soc News* 1980; 6:11-19.
- 12 Juniper EF, Frith PA, Dunnett C, Cockcroft DW, Hargreave FE. Reproducibility and comparison of responses to inhaled histamine and methacholine. *Thorax* 1978; 33:705-10.
- 13 Empey DW, Laitinen LA, Jacobs L, Gold WM, Nadel JA. Mechanisms of bronchial hyperreactivity in normal subjects after upper respiratory tract infection. *Am Rev Respir Dis* 1976; 113:131-39.
- 14 Boulet L-P, Cartier A, Thomson NC, Roberts RS, Dolovich J, Hargreave FE. Asthma and increases in nonallergic bronchial responsiveness from seasonal pollen exposure. *J Allerg Clin Immunol* 1983; 71:399-406.
- 15 Golden JA, Nadel JA, Boushey HA. Bronchial hyperresponsibility in healthy subjects after exposure to ozone. *Am Rev Respir Dis* 1978; 118:267-94.
- 16 Holtzman MJ, Cunningham JH, Sheller JR, Irsigler GB, Nadel JA, Boushey HA. Effect of ozone on bronchial reactivity in atopic and nonatopic subjects. *Am Rev Respir Dis* 1979; 120:1056-67.
- 17 Orehek J, Massan JP, Gayraud P, Grimaud C, Charpin J. Effect of short-term, low-level nitrogen dioxide exposure on bronchial sensitivity of asthmatic patients. *J Clin Invest* 1976; 57:301-07.
- 18 Cockcroft DW, Ruffin RE, Frith PA, Cartier A, Juniper EF, Dolovich J, et al. Determinants of allergen-induced asthma: dose of allergen, circulating IgE antibody concentration, and bron-



- chial responsiveness to inhaled histamine. *Am Rev Respir Dis* 1979; 120:1053-58
- 19 Dahms TE, Bolin JF, Slavin RC. Passive smoking: effect on bronchial asthma. *Chest* 1981; 80:530-34
  - 20 Shephard RJ, Collins R, Silverman F. Passive exposure of asthmatic subjects to cigarette smoke. *Environ Res* 1979; 20:392-402
  - 21 Cartier A, Malo JL, Begin P, Sestier M, Martin RR. Time course of the bronchoconstriction induced by inhaled histamine and methacholine. *J Appl Physiol* 1983; 54:821-26
  - 22 Virgulto J, Bouhuys A. Electronic circuits for recording of maximum expiratory flow-volume (MEFV) curves. *J Appl Physiol* 1973; 35:145-47
  - 23 Ramieri Jr A, Jatlow P, Seligson D. New method for rapid determination of carboxyhemoglobin by use of double-wavelength spectrophotometry. *Clin Chem* 1974; 20:278-81
  - 24 Stewart RD. The effects of low concentrations of carbon monoxide in man. *Scand J Respir Dis* 1974; 91(suppl):56-62
  - 25 Jones RM, Fagan R. Carboxyhemoglobin in nonsmokers: a mathematical model. *Arch Environ Health* 1975; 30:184-89
  - 26 Peterson JE, Stewart RD. Absorption and elimination of carbon monoxide by inactive young men. *Arch Environ Health* 1970; 21:165-71
  - 27 US Department of Health, Education and Welfare. Smoking and health: A report of the Surgeon General. DHEW Publication No. (PHS) 79-50066. 1979
  - 28 Cryer PE, Haymond MW, Santiago JV, Shah SD. Norepinephrine and epinephrine release and adrenergic mediation of smoking-associated hemodynamic and metabolic events. *N Engl J Med* 1976; 295:373-77
  - 29 Russell MAH, Feyerabend C. Blood and urinary nicotine in nonsmokers. *Lancet* 1975; 1:179-81
  - 30 Matsukura S, Taminato T, Kitano N, Seino Y, Hamada H, Uchihashi M, et al. Effects of environmental tobacco smoke on urinary cotinine excretion in nonsmokers: evidence for passive smoking. *N Engl J Med* 1984; 311:818-32
  - 31 Wallis TW, Rogers WR, Johnson WC Jr. Effects of acute and chronic exposure to nicotine aerosol on bronchial reactivity to inhaled methacholine. *J Appl Physiol* 1982; 52:1071-76
  - 32 Simonsson BG. Clinical and physiological studies on chronic bronchitis. III. Bronchial reactivity to inhaled acetylcholine. *Acta Allergologica* 1965; 20:325-48
  - 33 Brown R, Ingram RH Jr, Wellman JJ, McFadden ER Jr. Effects of intravenous histamine on pulmonary mechanics in nonasthmatic and asthmatic subjects. *J Appl Physiol* 1977; 42:221-27
  - 34 Spector SL, Luparello TJ, Kopetzky MT, Souhrada J, Kinsman RA. Response of asthmatics to methacholine and suggestion. *Am Rev Respir Dis* 1976; 113:43-50
  - 35 Spector SL, Kinsman RA. More implications of reactivity characteristics to methacholine and histamine in asthmatic patients. *J Allerg Clin Immunol* 1979; 64(part 2):587-89
  - 36 Gerrard JW, Cockcroft DW, Mink JT, Cotton DJ, Poonarvala R, Dosman JA. Increased non-specific bronchial reactivity in cigarette smokers with normal lung function. *Am Rev Respir Dis* 1980; 122:577-81
  - 37 Malo JL, Filiatrault S, Martin RR. Bronchial responsiveness to inhaled methacholine in young asymptomatic smokers. *J Appl Physiol* 1982; 52:1464-70
  - 38 Buczek GB, Day A, Vanderdoelen JL, Boucher R, Zamel N. Effects of cigarette smoking and short-term smoking cessation on airway responsiveness to inhaled methacholine. *Am Rev Respir Dis* 1984; 129:12-14
  - 39 Leeder SR, Corkhill RT, Irving LM, Holland WW, Colley JRT. Influence of family factors on asthma and wheezing during the first five years of life. *Br J Prev Soc Med* 1976; 30:213-18
  - 40 Gortmaker SL, Walker DK, Jacobs FH, Ruch-Ross H. Parental smoking and the risk of childhood asthma. *Am J Pub Health* 1982; 72:574-79
  - 41 Becker CG, Dubin T, Wiedemann HP. Hypersensitivity to tobacco antigen. *Proc Natl Acad Sci* 1976; 73:1712-16
  - 42 Lehrer SB, Barbandi F, Taylor JP, Salvaggio JE. Tobacco smoke "sensitivity"—is there an immunologic basis? *J Allerg Clin Immunol* 1984; 73:240-45

2023379562

**2023379563**

Stankus, R.P., Menon, P.K., Rando, R.J., Glindmeyer, H., Salvaggio, J.E., Lehrer, S.B. "Cigarette smoke-sensitive asthma: Challenge studies" J Allergy Clin Immunol 82: 331-338, 1988.

**SUMMARY:** The effects of exposure to environmental tobacco smoke on pulmonary function were assessed in 21 subjects with asthma who claimed respiratory complaints (cough, shortness of breath, and chest tightness) on previous exposure to cigarette smoke. Exposure to mechanically produced tobacco smoke was performed in a static inhalation chamber for two 2-hour intervals at two distinct smoke levels (as measured by carbon monoxide, nicotine, and particulate levels). Seven of the 21 smoke-challenged subjects experienced a significant ( $>20\%$ ) decline in FEV1 during passive exposure to tobacco smoke. One of these seven subjects was nonatopic, whereas a second subject had a negative response to methacholine challenge. The smoke-challenge responses were reproducible in all seven reactive subjects. Increasing concentrations of tobacco smoke failed to elicit pulmonary changes in previously challenged, unreactive or "smoke-tolerant" subjects. There was no association between a positive smoke challenge and the presence of serum IgE antibodies and/or a positive immediate wheal-and-flare skin test to a tobacco leaf extract. Collectively, these studies document a significant decline in pulmonary function in a substantial percentage (33%) of a population of "smoke-sensitive" subjects with asthma exposed to environmental tobacco smoke. The data also dissociate this effect from tobacco-leaf hypersensitivity.

2023379564

## Cigarette smoke-sensitive asthma: Challenge studies

Richard P. Stankus, PhD, MD, Prem K. Menon, MD, Roy J. Rando, ScD,  
Henry Glindmeyer, DEng, John E. Salvaggio, MD, and  
Samuel B. Lehrer, PhD New Orleans, La.

*The effects of exposure to environmental tobacco smoke on pulmonary function were assessed in 21 subjects with asthma who claimed respiratory complaints (cough, shortness of breath, and chest tightness) on previous exposure to cigarette smoke. Exposure to mechanically produced tobacco smoke was performed in a static inhalation chamber for two 2-hour intervals at two distinct smoke levels (as measured by carbon monoxide, nicotine, and particulate levels). Seven of the 21 smoke-challenged subjects experienced a significant (>20%) decline in FEV<sub>1</sub> during passive exposure to tobacco smoke. One of these seven subjects was nonatopic, whereas a second subject had a negative response to methacholine challenge. The smoke-challenge responses were reproducible in all seven reactive subjects. Increasing concentrations of tobacco smoke failed to elicit pulmonary changes in previously challenged, unreactive or "smoke-tolerant" subjects. There was no association between a positive smoke challenge and the presence of serum IgE antibodies and/or a positive immediate wheal-and-flare skin test to a tobacco leaf extract. Collectively, these studies document a significant decline in pulmonary function in a substantial percentage (33%) of a population of "smoke-sensitive" subjects with asthma exposed to environmental tobacco smoke. The data also dissociate this effect from tobacco-leaf hypersensitivity. (J ALLERGY CLIN IMMUNOL 1988;82:331-8.)*

Results of several attempts to define the effects of passive cigarette-smoke exposure on lung function in subjects with asthma have been contradictory. In some studies, no subjects with asthma experienced significant declines in pulmonary function,<sup>1,2</sup> but in another study, subjects with asthma demonstrated a significant (>20%) fall in FEV<sub>1</sub> after exposure to ETS.<sup>3</sup> Certain limitations in study design presumably contribute to the discrepancy in results obtained from these previous studies. Therefore, we designed the present study to address these criticisms and answer the question, Can exposure to tobacco smoke produce a significant decline in pulmonary function in "smoke-sensitive" subjects with asthma?

### Abbreviations used

ETS: Environmental tobacco smoke  
TLE: Tobacco-leaf extract  
CO: Carbon monoxide

## MATERIAL AND METHODS

### Subjects

Twenty-one adult subjects with asthma who claimed exacerbation of their asthma on ETS exposure were recruited for study. Study subjects ranged in age from 21 to 50 years and included 16 female and five male subjects. Participants were chosen from respondents to a newspaper advertisement announcing the study. The absolute criterion for selection was a diagnosis of asthma that subjectively was exacerbated by exposure to ETS (i.e., "smoke-sensitive" asthma). The diagnosis of asthma was made previously by the subject's personal physician. Thirteen subjects were nonsmokers and eight were exsmokers (cessation of smoking more than 1 year). All 21 subjects claimed chest symptoms (chest tightness, shortness of breath, and cough) on exposure to ETS. Nineteen of the 21 subjects were atopic with asthma, as defined by immediate wheal-and-flare skin test reactivity

From the Sections of Allergy and Clinical Immunology and Pulmonary Diseases, Department of Medicine, Tulane Medical School, New Orleans, La.

Supported by a Special Project grant from the Council for Tobacco Research.

Received for publication Sept. 14, 1987.

Accepted for publication Jan. 20, 1988.

Reprint requests: Richard P. Stankus, PhD, MD, Tulane Medical School, 1700 Perdido St., New Orleans, LA 70112.

2023379565

to two or more common inhalant allergens from a skin test panel of 20 common seasonal and environmental allergens (e.g., house dust, mite, ragweed, grasses, and trees). Nineteen subjects had a positive methacholine challenge and two subjects did not. The methacholine challenge test was conducted by delivering sequential doses of methacholine in phenol-buffered saline solution (0.06, 0.12, 0.25, 0.50, 1.0, 2.0, 4.0, 8.0, 16.0, and 32.0 mg/ml) via mouthpiece with a DeVilbiss (DeVilbiss Co., Somerset, Pa.) No. 45 nebulizer. Each nebulizer was attached to compressed air at 20 psig producing, with the air vent closed, an outlet flow of  $11.0 \pm 0.1$  L/min. The length of each nebulization was controlled by a nebulization dosimeter (Rosenthal-French dosimeter, Johns Hopkins University, Baltimore, Md.) at a setting of 0.6 sec per inhalation. The mean output for each nebulizer varied between 43.3 and 47.1  $\mu$ l of solution per five inhalations with an intranebulizer variability between 0.9% and 5.3%. Subjects wore noseclips during methacholine challenge. Each dose was delivered during 2 minutes of normal tidal breathing. The FEV<sub>1</sub> was determined with a Pulmonaire (Jones Medical Instrument Co., Oak Brook, Ill.) spirometer at 0.5 and 4 minutes after each dose. If at either time there was a 20% or more fall in FEV<sub>1</sub> from the baseline prechallenge value, the test was terminated. If the FEV<sub>1</sub> did not decrease by this amount, then the next dose was delivered. The cumulative dose of methacholine that corresponded to a 20% decrease in FEV<sub>1</sub> was determined by linear interpolation of the last two points on the dose-response curve. This provocative dose of methacholine that causes a 20% decrease in FEV<sub>1</sub> is the PD<sub>20</sub>.

### Cigarette smoke-inhalation challenge

The general challenge protocol consisted of an initial history and physical examination of the study subjects and their completion of a questionnaire regarding smoking habits, symptoms of asthma, and atopic background together with symptoms experienced on exposure to ETS. After allergen skin testing and methacholine challenge, the 21 subjects were scheduled for cigarette smoke-inhalation challenge. Participants were instructed to avoid theophylline and oral/sympathomimetic medications for 24 hours before challenge. Inhaled bronchodilators were stopped 8 to 12 hours before each test, in accordance with established guidelines. Only three subjects were taking oral or inhaled steroids (prednisone, 7.5 mg each morning, or beclomethasone, two puffs four times daily), and this medication was withheld the morning of challenge. All subjects underwent cigarette-smoke challenge while their asthma was "stable" (i.e., no recent [less than 3 months] asthma flares, hospitalizations, upper respiratory tract infections, or significant adjustments in asthma medications).

After informed consent, as outlined by the Tulane University Human Investigation Committee, the subjects entered a static inhalation chamber (12 by 7 by 11 feet) in which a temperature of 21°C and relative humidity of 50% were maintained. Baseline pulmonary function testing (FEV<sub>1</sub>, FVC, and peak flow) was performed in the chamber with a Pulmonaire spirometer and Wright peak-flow meter. The subjects were then exposed for 2 hours to the cigarette-

smoke particulate level of approximately 400 cpm produced initially by igniting two cigarettes and, subsequently, by lighting additional cigarettes in order to maintain this level. Cigarettes (IR2F research cigarettes, American Tobacco Institute) were "smoked" via a Borgwaldt fully automatic smoking machine (Heinrich Borgwaldt, Hamburg, West Germany). In general, 7 to 10 cigarettes were ignited and burned during this "low-level" exposure. Triplicate measurements of FEV<sub>1</sub> were obtained at 30-minute intervals during cigarette-smoke challenge. Data are expressed as the single best effort to the three determinations for each time interval. Routinely, there was <5% difference in FEV<sub>1</sub> among any three determinations. If a significant (>20%) decline in FEV<sub>1</sub> was not induced by this first challenge, the subjects were allowed to exit the chamber, rest for a period of 30 minutes, and then reenter the chamber for a second smoke challenge of 2 hours. This second "high-level" exposure began by igniting four cigarettes and subsequently burning additional cigarettes to maintain a cigarette smoke-particulate level of approximately 800 cpm. A total of 15 to 19 cigarettes was burned to maintain this "high-level" exposure. If a significant decline in FEV<sub>1</sub> did not occur after this second challenge, the subjects were allowed to exit from the chamber, and the challenge procedure was terminated. Those subjects who experienced a significant fall in FEV<sub>1</sub> were removed from the inhalation chamber and administered a nebulized treatment with metaproterenol and/or a subcutaneous injection of epinephrine followed by repeat pulmonary function testing. All subjects were allowed to exit the chamber and terminate the challenge if at any time the exposure conditions became intolerable. No subject requested termination of the challenge.

### Quantitation of cigarette-smoke exposure during inhalation challenge

The level of cigarette-smoke exposure during bronchoprovocation studies was determined by measuring the CO, nicotine, and total particulate levels in the inhalation chamber during challenge with "low-level" and "high-level" cigarette smoke. Both mainstream and sidestream smoke were produced. Mainstream smoke was passed through a tube packed with glass fibers, thus removing some of the particulate phase but presumably little of the gas-phase components, such as CO and nicotine. Airborne particulate levels were used as the primary indicator of smoke concentration and were continuously monitored with a Sibata (MDA Scientific, Lincolnshire, Ill.) model P5H2 light-scattering aerosol indicator. Sample air was constantly pulled through the aerosol monitor with an external vacuum pump and critical orifice operating at a flow rate of 0.43 L/min. The particulate target levels as measured by this instrument were 400, 800, and, in a selected population of subjects, 1600 cpm for the 2, 4, and 8 cigarette challenges, respectively.

In addition to continuously monitoring the particulate levels with the light-scattering instrument, integrated samples were collected for gravimetric quantitation of particulate concentration. Samples were collected during the entire 2-hour challenge period with 37 mm type FA nonstick filters (Millipore Corp., Bedford, Mass.) contained in two-

2023379566

TABLE I. Characterization of smoke-challenge atmospheres

	Smoke level		
	"Low-level"	"High-level"	"Ultra-high level"
No. cigarettes smoked	9.4 $\pm$ 1.5	17.0 $\pm$ 2.5	28.6 $\pm$ 5.7
Concentration CO (ppm)	8.7 $\pm$ 1.7	13.3 $\pm$ 3.2	14.1 $\pm$ 4.8
Aerosol (cpm)	439 $\pm$ 53	895 $\pm$ 77	1742 $\pm$ 147
Aerosol ( $\mu\text{g}/\text{m}^3$ )	852 $\pm$ 52	1421 $\pm$ 300	ND
Nicotine ( $\mu\text{g}/\text{m}^3$ )	180 $\pm$ 44	439 $\pm$ 121	ND

ND = not done.

piece polystyrene cassettes. Flow rate through the filters was 1 L/min with SKC (SKC, Inc., Pittsburgh, Pa.) model 224 constant flow pumps. The filters were weighed before and after sampling on either a Mettler model H51AR (Mettler Instrument Corp., Highstown, N.J.) analytical balance or a Cahn electrobalance (Cahn Instruments Inc., Cerritos, Calif.), and the gravimetric concentration of airborne particulate was calculated in units of micrograms per cubic meter. Additionally, several filters were desorbed with 4.0 ml of methanol after weighing. The optical density of the methanol solution was measured at a wavelength of 325 nm with 1 cm quartz spectrophotometric cells. The absorbance was then correlated with mass of collected particulate and used to estimate the gravimetric concentration of selected filter samples.

CO levels were monitored with a Miran (Foxboro Co., Foxboro, Mass.) 1A gas infrared spectrophotometer. The instrument was operated at a wavelength of 4.7  $\mu\text{m}$  with a path length of 20.25 m. The manufacturer's calibration factor was used to convert optical absorbance measurements to parts per million concentration units. Before the generation of smoke in the inhalation chamber, the instrument was zeroed with room air; thus, the observed CO levels represent the amounts generated via smoking over and above the normal background ambient levels of CO.

Quantitation of airborne nicotine levels was based on the method of National Institute for Occupational Safety and Health.<sup>5</sup> Samples were collected on commercially available XAD-4 sorbent tubes (SKC, catalog No. 226-30-11-04) at a flow rate of 0.1 L/min. Sample duration was limited to 1 hour. After sampling, the XAD-4 tubes were desorbed with 1.0 ml of 0.01% triethylamine in ethyl acetate plus 50  $\mu\text{l}$  of a quinoline solution (10.0  $\mu\text{l}/\text{ml}$  in ethyl acetate) added as an internal standard. The samples were analyzed by gas chromatography on a Hewlett-Packard model 5880A chromatograph (Hewlett-Packard Co., Palo Alto, Calif.) with a nitrogen-phosphorus detector. The column was a fused silica capillary, 30 m by 0.53 mm, coated with a 1.5  $\mu\text{m}$  film of DB-5 (5% phenylmethylpolysiloxane, J & W Scientific, Inc., Rancho Cordova, Calif.). The carrier gas was helium at a flow rate of 15 ml/min. Oven temperature was programmed from 150° C to 175° C at 5° C per minute, with no initial hold time. The injector temperature was 250° C. Injection volumes were 2.0  $\mu\text{l}$ . The ratio of the

areas of the nicotine and quinoline peaks was compared to a standard curve generated from serial dilution of a nicotine stock solution for quantitation.

### Skin and RAST testing with TLE

All 21 subjects were prick skin tested with a commercial TLE (Greer Laboratories, Lenoir, N.C.) and a TLE prepared in our laboratory from the tobacco contents of research cigarettes (IR2F) provided by the Tobacco Institute.<sup>6</sup> Briefly, the tobacco was suspended in sterile 0.1 mol/L of phosphate-buffered saline (pH 7.4) and mixed overnight at 4° C. The suspension was centrifuged at 1400 g for 15 minutes, and the supernatant was dialyzed against either distilled water or borate buffer (0.2 mol/L, pH 8.0) for use in the RAST. Direct RAST was performed with the use of CNBr-activated paper disks for the detection of IgE antibodies to TLE.<sup>7</sup> For the RAST, antigen was coupled to disks at 1 mg per disk. For the test, 100  $\mu\text{l}$  of the subject's serum was incubated overnight with an allergen disk. After washing with physiologic saline, disks were incubated overnight with 100  $\mu\text{l}$  of <sup>125</sup>I-labeled anti-IgE antiserum (Kallestad Laboratories, Austin, Texas) (25,000 cpm), washed with saline to remove unreacted material, and counted in a Beckman (Beckman Instruments Inc., Irvine, Calif.) gamma counter to determine radioactivity in counts per minute bound to the disks. For evaluation of results, a RAST percent binding was obtained by dividing the counts per minute of test disks by counts per minute of <sup>125</sup>I-labeled anti-IgE added.

### RESULTS

#### Quantitation of cigarette-smoke exposure during inhalation challenge

Before inhalation challenge, the "level" of tobacco-smoke exposure in the environmental chamber was quantified after the initial combustion of either two or four cigarettes ("low-dose" and "high-dose" levels). For a selected population of subjects, the room was filled with cigarette smoke generated by initially igniting eight cigarettes.

The means and standard deviations of the parameters used to characterize the smoke challenge atmospheres are listed in Table I. Good correlation was

2023379567

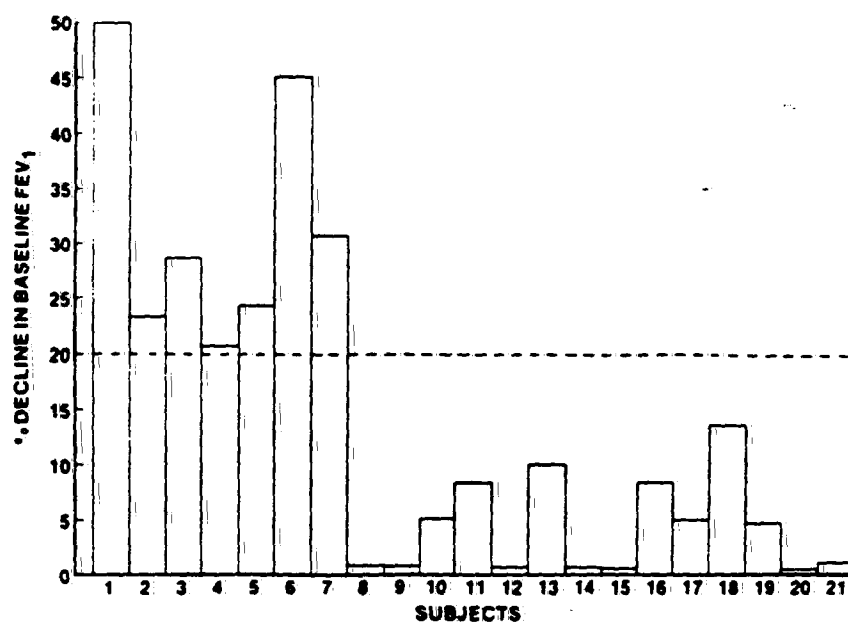


FIG. 1. Percent decline in FEV<sub>1</sub> of 21 "smoke-sensitive" subjects with asthma. Each bar graph represents the greatest decline from baseline FEV<sub>1</sub> during "high-level" and/or "low-level" challenge. Briefly, the change in FEV<sub>1</sub> represents the best effort of three determinations of FEV<sub>1</sub> obtained at 30-minute intervals during a single or two 2-hour passive cigarette-smoke exposures and recorded during the time interval of maximal decline from baseline FEV<sub>1</sub> (see text for details).

observed between the number of cigarettes and the two measures of particulate matter as well as the nicotine level. A relatively poor correlation was found with the CO levels.

#### Symptoms and pulmonary-function changes during ETS exposure

Eye irritation was experienced by all tested subjects. Nasal congestion and postchallenge sinus headache were also experienced by several subjects. Cough, dyspnea, and/or chest tightness were elicited in all subjects who experienced significant declines in FEV<sub>1</sub>.

Seven of the 21 smoke-challenged subjects demonstrated a significant (>20%) fall in FEV<sub>1</sub> on passive exposure to cigarette smoke (Fig. 1). Peak expiratory flow rates and FVC demonstrated similar declines, and there was good correlation between changes in FEV<sub>1</sub> and peak flow rates. There was no association between severity of asthma as judged by baseline FEV<sub>1</sub>, PD<sub>20</sub>, medications required to control disease, or number of hospitalizations per year and the occurrence of a positive cigarette-smoke challenge (Table II). Two of these reactive subjects responded to the initial "low-level" cigarette exposure (total of eight cigarettes burned in 2 hours), whereas the remaining five subjects reacted to the second "high-level" ex-

posure only (total of 16 cigarettes burned in 2 hours). The results of two of these positive smoke challenges are depicted in Figs. 2 and 3. The positive response produced 90 minutes during smoke inhalation ("low-level") in a "smoke-sensitive" subject with asthma is illustrated in Fig. 2. FEV<sub>1</sub> declined to 50% of baseline at 2 hours of smoke inhalation. This response was completely reversed within 15 minutes of administration of epinephrine and metaproterenol. Indeed, FEV<sub>1</sub> improved above baseline, suggesting a degree of pulmonary obstruction before the inhalation of cigarette smoke. The response elicited in a subject who was unreactive to methacholine challenge on both of two distinct testing days (6 months apart) is illustrated in Fig. 3. In this subject, a significant decline in FEV<sub>1</sub> occurred 30 minutes after "high-level" tobacco-smoke exposure. All seven smoke-reactive subjects reversed their pulmonary obstruction after administration of a bronchodilator (metaproterenol and/or epinephrine). Moreover, all seven reactive subjects experienced similar significant declines in FEV<sub>1</sub> when they were re-challenged with tobacco smoke on subsequent days (data not presented).

Fourteen of the 21 subjects with asthma who claimed worsening of their asthma on exposure to cigarette smoke before challenge did not experience a significant fall in FEV<sub>1</sub> (Fig. 1). All 14 subjects

2023379568

TABLE II. Characteristics of cigarette smoke-sensitive subjects with asthma

Smoke-challenge positive				Smoke-challenge negative			
Pt. No.	Age/Sex	Meds	PD <sub>20</sub> <sup>a</sup>	Pt. No.	Age/Sex	Meds	PD <sub>20</sub> <sup>a</sup>
1	39/M	T,B,A,S	0.3	8	42/F	T	8.0
2	34/F	T,B,C	2.0	9	39/F	B	2.3
3	50/F	B	12.0	10	24/F	B	1.0
4	34/F	B	Neg	11	33/F	B	60.0
5	34/M	T,B,A	1.8	12	31/M	B	Neg
6	38/F	T,B	0.6	13	26/F	T,B,S	50.0
7	42/F	T,B,S	3.8	14	33/F	B	5.0
				15	39/M	B,A,C	1.3
				16	26/F	B	8.0
				17	34/F	T,B	8.0
				18	21/F	T,B	0.8
				19	25/M	T	5.0
				20	25/F	T	5.0
				21	25/F	B	0.8

Pt. = patient; meds = medications; T = theophylline; B = bronchodilator (sympathetic); A = antihistamine; S = steroid; C = cromolyn; neg = negative.

<sup>a</sup>Cumulative dose of methacholine in breath units. One breath unit equals one inhalation of a dosimeter-delivered puff of a methacholine solution of concentration 1 mg/ml.

tolerated exposure to both "low-level" and "high-level" cigarette smoke. Five of these subjects related such a strong history of cigarette-smoke sensitivity that they were rechallenged on a separate day to "ultra-high" levels of cigarette smoke produced by burning approximately 24 cigarettes in a 2-hour period (particulate level, 1600 cpm). Again, none of these five subjects experienced a significant fall in FEV<sub>1</sub> on cigarette-smoke exposure.

#### RAST and skin test reactivity to TLE

TLE reactivity was assessed in all 21 subjects. Ten of the 21 study subjects demonstrated positive wheal-and-flare skin test reactivity (a wheal diameter 3 mm greater than saline-induced control wheal) to both a commercial TLE and one prepared in our laboratory. Sera from seven of these subjects were reactive by RAST to TLE (Table III). There was no association between skin test or RAST reactivity to TLE and the induction of a positive cigarette-smoke challenge.

#### DISCUSSION

This study was designed to answer whether exposure to tobacco smoke produces a significant decline in pulmonary function in subjects with asthma. Although at least three previous studies have examined the effects of ETS on both pulmonary function and airway reactivity in subjects with asthma, their conflicting results together with important limitations in study design prompted the present analysis.

Shephard et al.<sup>1</sup> assessed the symptoms and airway responses of a group of 14 adults with asthma passively exposed to controlled concentrations of cigarette smoke. Smoke exposure consisted of a single 2-hour passive exposure to cigarette smoke produced by igniting a total of seven cigarettes. These exposure conditions generated and maintained a CO concentration of 24 ppm above ambient and a suspended particulate concentration of 2 to 4 mg/m<sup>3</sup>. Changes of pulmonary function were slight in all exposed subjects, and dynamic lung volumes, including FEV<sub>1</sub>, were unaltered. Significantly, only four of the 14 tested subjects claimed respiratory sensitivity to cigarette smoke before challenge.

Dahms et al.<sup>3</sup> exposed 10 subjects with bronchial asthma and 10 control subjects to sidestream cigarette smoke for 1 hour in an environmental chamber. Subjects were exposed to cigarette smoke that produced a CO level of 15 to 20 ppm. The group with asthma demonstrated a significant linear decrease in pulmonary function during this exposure. After 1 hour, FEV<sub>1</sub> decreased 21% in the subjects with asthma. The control subjects demonstrated no change in pulmonary function when they were exposed to identical conditions. Unfortunately, only group mean data were reported, and it is not possible from the data to determine if all or only a fraction of the group with asthma experienced a  $\geq 20\%$  decline in FEV<sub>1</sub>.

Recently, Wiedemann et al.<sup>2</sup> studied the acute effects of 1 hour of passive cigarette-smoke exposure

2023379569



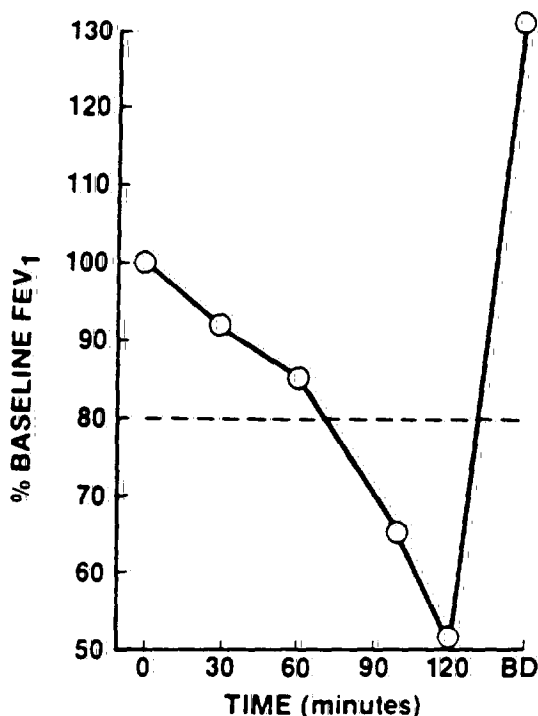


FIG. 2. Decline in baseline FEV<sub>1</sub> produced during "low-level" smoke exposure in a "smoke-sensitive" subject with asthma. Circles represent the highest of three determinations of FEV<sub>1</sub> at each time interval during smoke challenge. BD, point of time of administration of bronchodilator.

(CO level 40 to 50 ppm) on lung function and airway reactivity of nine adults with asthma. Six of the nine subjects with asthma claimed that cigarette smoke "bothered" their asthma. ETS exposure produced no significant change in expiratory flow rates and a small decrease in nonspecific bronchial reactivity.

All the above studies possess similar characteristics of their patient population and study design that differ significantly from our study. First, these earlier studies used relatively small numbers of subjects with asthma, of which only a fraction complained of worsening of their asthma on passive exposure to cigarette smoke. Of even greater consequence, however, previous challenge studies have been limited in that only a single 1- or 2-hour exposure to tobacco smoke was performed.

The present study challenged 21 "smoke-sensitive" subjects with asthma, many of whom were challenged with cigarette smoke on multiple occasions. All seven of the "smoke-reactive" subjects were rechallenged on separate days and demonstrated reproducible declines in FEV<sub>1</sub>. Similarly, five of the nonreactive "smoke-tolerant" subjects with asthma were chal-

lenged multiple times at varying smoke concentrations with no change in FEV<sub>1</sub>. Perhaps the most important and distinctive feature of our study design was the use of two 2-hour exposures during smoke challenge. Indeed, if length of exposures similar to previous studies (single, 1-, or 2-hour challenges) were used in the present study, none or at most two of the seven "smoke-reactive" subjects with asthma would have been identified. No subject experienced a significant fall in FEV<sub>1</sub> during the first hour of challenge, and five subjects were reactive to only the 2-hour "high-level" challenge. Clearly, in our study, length of exposure to ETS represents an important parameter in defining "smoke reactivity."

Challenge conditions (length and "level" of exposure to cigarette smoke) designed for the present study appeared adequate to distinguish subjects whose asthma was exacerbated on exposure to cigarette smoke. Indeed, five subjects who did not experience a significant fall in FEV<sub>1</sub> under standard challenge conditions were exposed to levels of cigarette smoke that produced a particulate level of 1600 cpm (twice the original "high-level"). None of these subjects experienced a significant decline in FEV<sub>1</sub>. It is important to note that use of the phrases "low-level" and "high-level" to characterize the smoke environments used for challenge studies reflects levels of smoke exposure relative only to this study. These exposure conditions were representative of moderate to high "real-world" smoke-exposure environments. Virtually all the subjects with asthma, however, believed that they had been exposed to similar environmental conditions in the past.

Nicotine is generally considered to be the best marker for ETS, since there are no significant non-smoke sources of the material.<sup>8</sup> Both CO and particulate levels demonstrate significant contributions from normal ambient levels independent of smoking. In our experiments, background CO has been factored out of our measurements by zeroing the infrared monitor with challenge room air before smoking. Particulate levels do, however, reflect a contribution from normal background levels.

The particulate levels of 852 and 1421  $\mu\text{g}/\text{m}^3$  for the "low" and "high" level exposures, respectively, are within the upper range of levels identified in various surveys of taverns and game halls.<sup>9</sup> Likewise, the nicotine levels are also in the upper range of concentrations identified in public places (approximately 1 to 100  $\mu\text{g}/\text{m}^3$ ), although most of these measurements are in the range of 10  $\mu\text{g}/\text{m}^3$ .<sup>8</sup>

The CO levels measured during the challenges are comparable to measurements made during many surveys of public facilities. However, these are charac-

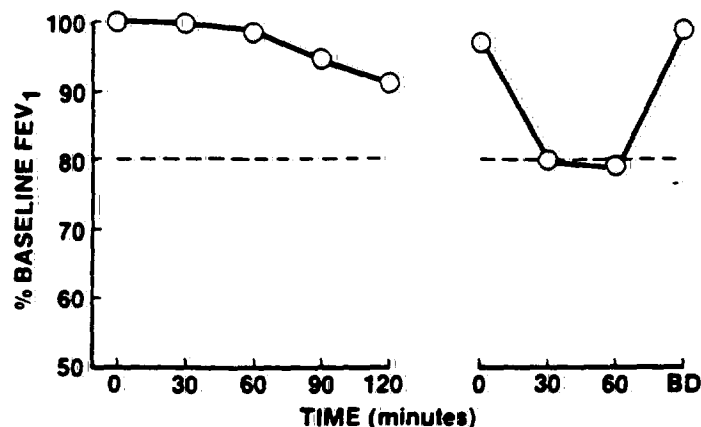


FIG. 3. Decline in baseline FEV<sub>1</sub> produced during "low-level" (left-hand side) and "high-level" exposure to tobacco smoke. Circles represent the highest of three determinations of FEV<sub>1</sub> at each time interval during smoke challenge. BD, point of time of administration of bronchodilator.

terized by variable results and are usually significantly influenced by background levels of CO produced by automotive emissions and other sources of combustion. Overall, the data indicate that the smoke levels generated for the challenge testing are considerably higher than normally found in such places as restaurants and offices but are within the range reported in crowded, poorly ventilated taverns, sports arenas, and closed automobiles.

The gradual declines in FEV<sub>1</sub>, recorded in all seven cigarette smoke-reactive subjects differ from both the early and late asthmatic responses induced by classic allergen inhalation testing. Accordingly, the mechanism(s) of cigarette smoke-induced bronchospasm remains unclear. Preliminary studies in our laboratory have failed to demonstrate an increase in serum histamine level in subjects with a positive smoke challenge. The contribution of neural pathways or "psychologic overlay" in the initiation of cigarette smoke-induced asthma cannot be excluded in the present study. Cigarette smoke might trigger emotional responses that may serve to aggravate an already existing respiratory problem. Although it is impossible to mask the smell of cigarette smoke and control for the psychologic effects of cigarette-smoke exposure, we did perform sham exposures by placing the subjects in the inhalation chamber and measuring FEV<sub>1</sub> during a 2-hour interval. No significant declines in FEV<sub>1</sub> were recorded in any of the subjects during this mock challenge.

Nineteen of the 21 subjects with asthma challenged in our study were atopic. Ten subjects demonstrated immediate prick skin test reactivity to both a commercial TLE and an extract prepared in our laboratory

TABLE III. Skin test and RAST reactivity to TLE

Pt. No.	ST*	RAST†	Smoke challenge
1	+	4.4	+
2	+	3.5	+
3	+	3.8	+
4	+	7.3	-
5	+	3.8	-
6	+	12.5	-
7	+	9.6	-
8	+	6.6	-
9	+	4.4	-
10	+	4.3	-
11	-	1.2	+
12	-	0.8	+
13	-	1.3	+
14	-	1.3	+
15	-	1.2	-
16	-	1.1	-
17	-	0.6	-
18	-	0.4	-
19	-	1.2	-
20	-	0.9	-
21	-	1.2	-

\*Immediate skin test reactivity.

†RAST percent binding.

from the tobacco contents of research cigarettes. Sera from seven of these 10 skin test-reactive subjects were positive by RAST to TLE. It has been suggested by results from at least one previous study<sup>10</sup> that tobacco-leaf reactivity is associated with cigarette-smoke sensitivity. This conclusion, however, was based on the

2023379571

results of subjective improvement after immunotherapy with TLE and did not include objective measurements of benefit. In the present study, we found no correlation between the presence of a positive RAST and/or immediate skin test reactivity to TLE and a significant decline in  $FEV_1$  on cigarette-smoke challenge. Therefore, these results do not support the use of TLE reactivity as an aid in the diagnosis of cigarette-smoke-sensitive asthma.

The tobacco plant belongs to the botanical family Solanaceae. Several foods, such as potatoes, tomatoes, eggplants, and green peppers, are also members of this botanical family. The tobacco leaf is a heterogeneous mixture of proteins, and there are multiple combustion products of tobacco that increase the complexity of antigen analysis. There are >2000 particulate, gaseous, and semivolatile components in tobacco smoke.<sup>11</sup> Therefore, defining the association of tobacco-smoke antigens/allergens with allergic respiratory disease must await the identification/isolation of appropriate substances for patient testing.

The results of this study demonstrate that a significant percentage (33%) of subjects with asthma who claim worsening of their asthma on passive exposure to ETS experience a >20% decline in  $FEV_1$  on smoke challenge. The reason(s) that the remaining two thirds of "smoke-sensitive" subjects with asthma do not experience objective changes in pulmonary function on exposure to ETS remains to be answered. It is conceivable that additional influences on pulmonary function (exercise or alcohol) may contribute to respiratory changes in association with ETS exposure.<sup>12</sup> A typical example would be subjects with asthma who are dancing and/or ingesting alcohol in a smoke-filled nightclub. An analysis of these additional, potentially aggravating influences is currently under investigation.

We thank Mr. M. Connor and Dr. M. Ogden of R. J. Reynolds Tobacco for assistance in the development of analytical methods for particulate matter and nicotine, and Josephine D. Stankus and Byron Lockhart for their expert technical assistance.

## REFERENCES

1. Shephard RJ, Collins R, Silverman F. "Passive" exposure of asthmatic subjects to cigarette smoke. *Environ Res* 1979; 20:392.
2. Wiedemann HP, Mahler DA, Loke J, et al. Acute effects of passive smoking on lung function and airway reactivity in asthmatic subjects. *Chest* 1986;89:180.
3. Dahms TE, Bolin JF, Slavin RG. Passive smoking: effects on bronchial asthma. *Chest* 1981;80:530.
4. Guidelines for bronchial inhalation challenges with pharmacologic and antigenic agents. *Am Thorac Soci News* 1980;6:11.
5. Method No. S293, NIOSH Manual of Analytical Methods, vol. 3. 2nd ed. U.S. Government Printing Office. DHHS publication no. 77-157-C.
6. Lehrer SB, Barbandi F, Taylor JP, Salvaggio JE. Tobacco smoke "sensitivity"—Is there an immunologic basis? *J ALLERGY CLIN IMMUNOL* 1984;73:240.
7. Ceska M, Lundkvist V. A new and simple radioimmunoassay for the determination of IgE. *Immunochemistry* 1972;9:1021.
8. Hinds WG, First MW. Concentrations of nicotine and tobacco smoke in public places. *N Engl J Med* 1975;292:844.
9. Sterling TD, Dimich H, Kobayashi D. Indoor byproduct levels of tobacco smoke: a critical review of the literature. *J Air Pollut Control Assoc* 1982;32:250.
10. Zussman BM. Tobacco sensitivity in the allergic population: a review with results of desensitization with 10 percent whole leaf tobacco extract. *Ann Allergy* 1980;45:304.
11. Norman V. An overview of the vapor phase, semivolatile and nonvolatile components of cigarette smoke. In: *Tobacco Chemists Research Conference*, vol. 30. Greensboro, N.C.: 1977: 5-7.
12. Lebowitz MD. Respiratory symptoms and disease related to alcohol consumption. *Am Rev Respir Dis* 1981;123:16.

2023379572

2023379573

Bailey, W.C., Richards, J.M., Manzella, B.A., Brooks, C.M., Windsor, R.A., Soong, S.J. "Characteristics and correlates of asthma in a university clinic population" Chest 98(4): 821-828, 1990.

SUMMARY: To contribute more comprehensive information about the characteristics of asthma, this article analyzed patients served by the University of Alabama at Birmingham Comprehensive Asthma Program. Their physicians rated one fifth of these patients as having "severe" asthma with the remainder about equally divided between "moderate" and "mild." One in two first received a diagnosis of asthma ten or more years previously. Common comorbidities were hypertension, obesity, rhinitis, bronchitis, sinusitis, and arthritis. One half had visited an emergency room or been hospitalized for asthma in the past year. Inhaled bronchodilators and continuous theophylline were the most commonly prescribed medications. Side effects, especially tachycardia and insomnia, were common and almost exclusively associated with theophylline or corticosteroid therapy. Spirometric assessment showed chronic airflow obstruction in those with more severe asthma. Prevalence of respiratory symptoms, intensity of medication regimen, incidence of side effects, and health care utilization increased as asthma severity increased.

2023379574

# Characteristics and Correlates of Asthma in a University Clinic Population\*

William C. Bailey, M.D., F.C.C.P.; James M. Richards, Jr., Ph.D.;  
Bryn A. Manzella, M.P.H.; C. Michael Brooks, Ed.D.;  
Richard A. Windsor, Ph.D., M.P.H.; and Seng-jaw Soong, Ph.D.

To contribute more comprehensive information about the characteristics of asthma, this article analyzed patients served by the University of Alabama at Birmingham Comprehensive Asthma Program. Their physicians rated one fifth of these patients as having "severe" asthma with the remainder about equally divided between "moderate" and "mild." One in two first received a diagnosis of asthma ten or more years previously. Common comorbidities were hypertension, obesity, rhinitis, bronchitis, sinusitis, and arthritis. One half had visited an emergency room or been hospitalized for asthma in the past year. Inhaled bronchodilators and continuous theophylline were the most com-

monly prescribed medications. Side effects, especially tachycardia and insomnia, were common and almost exclusively associated with theophylline or corticosteroid therapy. Spirometric assessment showed chronic airflow obstruction in those with more severe asthma. Prevalence of respiratory symptoms, intensity of medication regimen, incidence of side effects, and health care utilization increased as asthma severity increased. (Chest 1990; 98:821-28)

UAB-University of Alabama at Birmingham

Asthma in adults contributes substantially to morbidity, mortality, and health care costs in the United States. More than 3 percent of total outpatient visits are attributable to asthma.<sup>1</sup> In 1983 there were 459,000 hospitalizations for asthma and 3,440 deaths listing asthma on the death certificate as the underlying cause of death; an additional 4,000 deaths recorded asthma as a comorbidity factor.<sup>2</sup> The epidemiology of asthma is not completely understood, and recommendations for research to clarify this issue were presented in a recent review.<sup>3</sup> The present article is a step in addressing these recommendations.

The Comprehensive Asthma Program at the University of Alabama at Birmingham (UAB) was established in 1981 to coordinate diagnostic and therapeutic services for inpatient and outpatient adult asthma care. The present article summarizes characteristics of the adult asthma population who received outpatient care at UAB. We examined demographic characteristics, comorbidity, pulmonary function, asthma severity and symptoms, medication patterns, and health care utilization. Because UAB is a tertiary care institution,

these patients may not represent the population of adults with asthma in Birmingham and also may or may not be completely representative of populations at other university-based asthma care programs. Therefore, this report is no substitute for comprehensive epidemiologic studies, but it is an important step in developing baseline data for nonhospitalized adult populations receiving treatment for asthma.

## METHODS AND MATERIALS

### Subjects

Much of the data were collected in connection with a study funded by the National Heart, Lung, and Blood Institute (Bethesda, Md) to evaluate a special educational program designed to improve the self-management skills of adults with asthma.<sup>4,5</sup> Subjects were recruited from an overall pool of 479 adults who had received treatment in the UAB Asthma Program. Basic demographic and comorbidity data were collected for these patients from clinic records. Data with respect to asthma severity and duration were collected for a smaller set of 366 patients who were screened for participation in the clinical intervention during regular clinic visits. The primary data for the present research, however, were based on the 263 (73 percent) screened patients who meet the eligibility criteria listed below and were willing to participate. (Only 11 eligible subjects refused to participate.) Data were collected from those 263 patients through a combination of physician ratings, structured interviews, and questionnaires. The eligibility criteria included the following: (1) age 17 years or older; (2) recurrent episodes of wheezing or dyspnea; (3) sufficient history available to categorize asthma severity; (4) objective evidence of airway obstruction during episodes; (5) objective evidence of improved airflow when symptom free; (6) asthma severe enough to require some medication at the time of randomization; and (7) absence of chronic or debilitating disease that would compromise interpretation of data.

### Demographic Characteristics and Comorbidity

Data from clinic records were used to examine the basic charac-

\*From the Division of Pulmonary and Critical Care Medicine, University of Alabama at Birmingham (UAB); and the Veterans Affairs Medical Center, Birmingham (Dr. Bailey); the UAB Office of Educational Development (Drs. Richards and Brooks); the UAB Division of Pulmonary and Critical Care Medicine (Ms. Manzella); the Department of Health Behavior, UAB School of Public Health (Dr. Windsor); and the UAB Comprehensive Cancer Center (Dr. Soong).

This work was supported by the research funding from the Division of Lung Diseases, the National Heart, Lung, and Blood Institute Grant RO1HL31481-03.

Manuscript received December 11; revision accepted March 26.  
Reprint requests: Dr. Bailey, 700 South 19th Street, Birmingham, AL 35233.

tenistics of the patient population served by UAB. Demographic characteristics included sex, race, age, and marital status. Data were also obtained for the following major types of comorbidity: hypertension, obesity, rhinitis, bronchitis, sinusitis, arthritis, diabetes mellitus, and chronic obstructive pulmonary disease (COPD).

#### *Asthma Severity and Duration*

Asthma severity was assessed by the regular pulmonary physician of each patient screened for the self-management study. Physicians were asked only to classify each patient as having mild, moderate, or severe asthma, using specific written guidelines. These guidelines emphasized that physicians were to rate the severity of the underlying disease, not status during a particular episode. A series of studies yielded results strongly supporting the usefulness and appropriateness of these simple ratings.<sup>14</sup>

Asthma duration was assessed in terms of the number of years since the patient first received a diagnosis of asthma. We used a three-point scale with the following categories: (a) less than 10 years, (b) 10 to 29 years, and (c) 30 years or more.

#### *Baseline Research Interview*

A baseline research interview was conducted with each subject entered into the self-management study. This interview was structured to characterize each patient's asthma and its impact on life-style.\* Data are organized into the following categories: (1) background characteristics; (2) smoking patterns; (3) pulmonary function; (4) asthma symptoms; (5) respiratory illnesses and symptoms; (6) medication regimens, adherence, and side effects; and (7) health care utilization.

#### *Background Characteristics and Smoking Patterns*

The baseline interview included questions about the following background characteristics: educational level, number of children, employment status, and third-party coverage for medical care costs. Both active and passive smoking were assessed.

#### *Pulmonary Function*

Pulmonary functioning was measured through spirometric assessment. Three measures were obtained: (a) forced vital capacity (FVC), (b) forced expiratory capacity in 1's (FEV<sub>1</sub>), and (c) ratio of FEV<sub>1</sub> to FVC.

#### *Asthma Symptoms*

Two sets of measures were used by the patients to subjectively assess their asthma. The first consisted of six "bother scales" in which subjects rated the amount of distress caused by asthma on a four-point scale ranging from a score of 1 for "not at all bothered, no symptoms" to a score of 4 for "severely bothered, unable to function." The six scales assessed the extent to which patients "typically" were bothered in the winter, spring, summer, and fall, and the extent to which they had been bothered in the past seven days and in the past 24 hours.<sup>7</sup> The second measure used the Asthma Symptoms Checklist,<sup>8</sup> a 36-item Likert-type scale developed at the National Asthma Center-National Jewish Hospital<sup>9</sup> to analyze the incidence of five types of symptoms—airway obstruction, fatigue, irritability, panic-fear, and hyperventilation—during asthma attacks. Scores ranged from 1 for "never" occurring as part of an attack to 5 for "always" occurring.

#### *Respiratory Illnesses and Symptoms*

Subjects were asked whether they had experienced any episodes of the following respiratory illnesses during the past 12 months: (a) prolonged shortness of breath, (b) colds, upper respiratory tract infections, (c) spells of coughing, (d) bronchitis, and (e) pneumonia. Similarly, patients were asked if they had experienced the following respiratory symptoms during the past seven days: (a) shortness of

breath, (b) coughing, (c) wheezing, (d) decreased exercise tolerance, (e) increased sputum, (f) thick sputum, and (g) green or yellow sputum.

#### *Medication*

The interview provided information about whether the recommended medication regimen for each patient included (a) an inhaled bronchodilator, (b) continuous theophylline, (c) two or more courses of steroids in the past year, (d) some other inhaled medication, and (e) two or more courses of antibiotics in the past year. Two six-item scales assessed adherence to the recommended oral and inhaled medication regimens. These scales were based on the prototype scale described by Morrissey, et al.<sup>10</sup> The wording was changed slightly to be more applicable to asthma, and items were added to assess overuse.

Previous research has indicated that improper use of inhalers is a significant problem in adults with asthma.<sup>11</sup> Therefore, a ten-item observational checklist to assess inhaler use skills was developed and demonstrated to have good measurement characteristics.<sup>9</sup> Each of these three scales was scored in terms of whether each patient was adherent on *all* items in the scale. This score represents the desirable level of adherence, not an extraordinary level.

Medication side effects can be a significant problem in the management of adult asthma. Therefore, subjects were asked if they had experienced the following side effects in the past three months: (a) pounding heart (tachycardia), (b) insomnia, (c) nausea, (d) bad dreams, (e) white spots in the mouth (oral thrush), (f) seizures, and (g) "any other side effect of your asthma medicine."

#### *Health Care Utilization*

Poor self-management of adult asthma may produce overutilization of health care resources. To address this issue, subjects were asked if a respiratory problem had caused the following events during the past year: (a) telephone call to a physician, (b) office visit to a physician, (c) emergency room visit, and (d) hospitalization.

#### *Statistical Analysis*

The results are reported for the entire sample and, in most cases, they are broken down by asthma severity. In a few cases, the results are also broken down by duration of asthma or by type of medication. (Additional analyses that are not reported herein found no consistently significant impact of asthma duration on the various measures.) Differences were tested for statistical significance through  $\chi^2$  for categorical measures and through *F* or *t* tests for continuous measures. It should be remembered that the varying numbers of patients whose data are reported in the tables are due to whether or not patients visited the UAB clinic during the data collection period and to the eligibility and willingness of patients to participate in the clinical intervention. The *N*s also vary somewhat among variables because data were missing for some patients on specific variables (particularly on the Asthma Symptoms Checklist). However, no systematic differences are present between patients with such missing data and patients with complete data.

## RESULTS

Table 1 summarizes demographic characteristics and prevalence of comorbidity for asthma patients at UAB. Female patients predominated in the UAB population, confirming results of other studies of adult asthma clinics<sup>12</sup> but differing from most epidemiologic studies.<sup>14-18</sup> The proportion of whites in this study was consistent with the racial makeup of the population of the Jefferson County (Birmingham) area. The age distribution in the UAB clinic population was broad

Table 1—Demographic Characteristics and Comorbidity in Patients Served by the UAB Clinic\*

	Total Pool, % (N = 479)	Screened for Self-Mgmt Study (N = 366)		Entered into Self-Mgmt Study (N = 263)	
		%	$\chi^2$	%	$\chi^2$
Sex					
Female	66.4	67.2	0.47	65.8	0.10
Male	33.6	32.8		34.2	
Race					
White	65.1	67.4	3.55	67.3	1.22
Black	34.9	32.6		32.7	
Age, yr					
<30	19.7	16.4	13.81†	16.0	9.56‡
30-49	37.8	37.5		37.0	
50-69	30.7	33.7		35.9	
≥70	11.8	12.3		11.1	
Marital status					
Never married	22.1	19.7	5.65	18.3	5.26
Formerly married	16.5	16.4		17.6	
Currently married	61.4	63.4		64.1	
Comorbidity					
Hypertension	21.5	21.6	0.01	24.0	2.08
Obesity	9.8	9.3	0.48	9.5	0.06
Rhinitis	8.6	9.0	0.41	8.4	0.03
Bronchitis	8.6	8.5	0.02	8.0	0.25
Sinusitis	6.7	6.8	0.06	7.2	0.28
Arthritis	5.4	6.6	3.86‡	6.1	0.49
Diabetes mellitus	4.4	4.6	0.25	5.3	1.23
COPD	3.8	2.5	7.24†	1.9	5.56‡

\*Note:  $\chi^2$  compared screened and entered patients with the remainder of the total pool of patients.

† $p < 0.01$ .

‡ $p < 0.05$ .

with 42 percent of patients being age 50 years or older. Marital status percentages were consistent with the norms for the age and sex distributions.

Hypertension was the most common (22 percent) comorbidity factor. Obesity, rhinitis, bronchitis, sinusitis, and arthritis also were present in 5 percent or more of the patients. These results are consistent with the demographic characteristics of UAB patients and suggest that asthma patients are much like the general population in terms of the presence of various health problems.

Table 1 also compares the three groups of patients who provided data for this study. The results for the

Table 2—Asthma Severity and Duration in Patients Screened for the Self-Management Study (N = 319)

Years Since First Asthma Diagnosis	% of All Patients	% of Patients Whose Asthma Is			$\chi^2$
		Mild	Moderate	Severe	
<10	48.0	60.0	40.0	40.7	12.14*
10-29	35.1	28.0	40.0	39.0	
≥30	16.9	12.0	20.0	20.3	
Total	100	100	100	100	

\* $p < 0.05$ .

three groups are highly similar, with the only consistently significant differences indicating that screened and entered patients were less likely to fall in the youngest age category and less likely to have COPD. (Our eligibility criteria eliminated patients with severe chronic pulmonary obstruction.) Therefore, these results indicate that information based on screened and entered patients can be generalized to the UAB asthma population with considerable confidence.

Additional analyses for patients entered into the self-management study found no relationship between asthma severity and educational level, number of children, employment status, third-party health care coverage, smoking status, or exposure to passive smoking. Only 15.4 percent of the study population were current smokers, a substantially lower proportion than in the general population.<sup>19</sup> The study population included a substantial proportion of female former smokers (47.0 percent), indicating smoking cessation rates among this sample were higher than in the general population of female subjects.<sup>20</sup> With regard to passive smoking, we found that exposure at work was more common (for those who worked) than exposure at home.

Table 2 summarizes the relationship between asthma severity and asthma duration. The UAB physicians rated 40.2 percent of those patients as having mild asthma, 42.3 percent as having moderate asthma, and 17.5 percent as having severe asthma. The clearest trend in this table is that patients with milder disease

Table 3—Pulmonary Function in Patients Entered into the Self-Management Study

	FVC% of Predicted, Mean ± SD		FEV <sub>1</sub> % of Predicted, Mean ± SD		Ratio of FEV <sub>1</sub> to FVC, Mean ± SD	
All entered patients (N = 238)	76.0	19.5	69.0	23.5	72.8	14.1
Entered patients whose asthma is (N = 238)						
Mild	80.6	17.9	77.6	21.9	77.1	12.9
Moderate	74.7	19.4	68.3	21.7	74.1	12.0
Severe	69.8	21.2	53.5	23.0	60.5	14.9
F	4.92*		17.2*		24.8*	
Entered patients who have had asthma (N = 214)						
<10 yr	75.9	20.0	71.3	24.6	75.0	14.6
10-29 yr	77.3	20.2	68.7	23.4	71.8	13.7
30+ yr	73.7	15.6	62.3	18.6	68.4	13.2
F	0.39		1.77		3.04*	
Entered patients who smoked (N = 206)						
Never	76.4	18.6	70.9	21.3	74.6	12.7
Formerly	74.2	19.1	65.3	24.1	70.2	15.8
Currently	70.7	17.8	63.5	22.0	72.0	14.6
F	1.15		1.98		2.09	

\* $p < 0.01$ .



Table 4—Asthma Symptoms in Patients Entered into the Self-Management Study

	All Entered Patients. Mean $\pm$ SD		Entered Patients Whose Asthma Is:				F	
			Mild. Mean $\pm$ SD	Moderate. Mean $\pm$ SD	Severe. Mean $\pm$ SD			
Extent to which asthma symptoms have bothered patient (N = 249)								
During past 7 days	2.53	1.19	2.12	1.01	2.63	1.20	3.13	12.44*
In past 24 h	2.26	1.19	1.81	0.95	2.34	1.18	2.98	16.72*
Usually during the								
Spring	2.96	1.06	2.78	1.14	3.14	0.97	2.96	2.98
Summer	2.52	1.06	2.34	1.05	2.62	1.02	2.65	2.17
Fall	2.89	1.07	2.47	1.06	3.13	1.01	3.09	11.61*
Winter	2.61	1.13	1.46	1.10	2.93	1.08	3.23	6.36*
Frequency with which asthma attacks include symptoms of (N = 136)								
Airway obstruction	3.59	0.93	3.59	1.01	3.40	0.88	4.06	4.17*
Fatigue	3.23	1.21	3.31	1.27	2.98	1.23	3.71	3.13*
Irritability	2.63	1.03	2.73	1.17	2.31	0.87	3.24	7.41*
Panic and Fear	2.31	1.04	2.08	0.89	2.09	0.86	3.34	16.05*
Hyperventilation	1.94	0.78	1.97	0.90	1.88	0.66	2.05	0.41

\*p&lt;0.01.

†p&lt;0.05.

had had their conditions diagnosed more recently.

The results of spirometric assessments are summarized in Table 3. The overall pulmonary function means are low. There is a clear-cut relationship between the severity of asthma and level of impairment in both volumes and flow rates, but the flow rates, particularly the FEV<sub>1</sub>, show a significantly greater decline as asthma becomes more severe. These results support results from previous studies<sup>15</sup> that suggested that flow rates decrease with increasing number of years from diagnosis. There is no correlation between impairment in pulmonary function and passive smoking and only a slight correlation is seen between current smoking status and reduction in FEV<sub>1</sub>/FVC.

Results for asthma symptoms are summarized in Table 4. There is no clear-cut pattern of asthma symptoms being increasingly bothersome during the spring or summer; instead, fall and winter seem to be associated with more bothersome asthma symptoms in the UAB population. Symptoms experienced during the past seven days and the past 24 hours were a greater problem in patients with increasingly severe asthma. These results appear consistent with the data for asthma provided by the National Health Interview Survey.<sup>2</sup> The Asthma Symptoms Checklist results indicate that hyperventilation was seldom seen in the UAB population, but airflow obstruction, fatigue, irritability, and panicky reactions to asthma attacks

Table 5—Respiratory Illnesses and Symptoms in Patients Entered into the Self-Management Study

	% of All Entered Patients	% of Entered Patients Whose Asthma Is:			$\chi^2$
		Mild	Moderate	Severe	
Respiratory illnesses experienced in past 12 mo (N = 260)					
Prolonged shortness of breath	75.4	67.4	74.8	93.5	11.43*
Cold, upper respiratory tract infection	67.3	66.3	68.9	65.2	0.27
Spell of coughing	58.5	54.7	56.3	71.7	4.11
Bronchitis	40.0	36.8	43.0	37.0	1.25
Pneumonia	9.6	6.3	13.4	6.5	3.71
Respiratory symptoms experienced in past 7 days (N = 262)					
Shortness of breath	67.9	57.9	71.4	80.4	8.38*
Coughing	67.2	54.7	75.6	71.7	10.98*
Wheezing	65.6	50.5	71.4	82.6	17.29*
Decreased exercise tolerance	51.9	38.9	56.3	67.4	11.73*
Increased sputum	41.6	32.6	46.2	50.0	5.50
Thick sputum	30.2	23.2	31.1	43.5	6.10*
Green or yellow sputum	17.9	16.8	17.6	21.7	0.53

\*p&lt;0.01.

†p&lt;0.05.

Table 6—Medication Regimens and Adherence in Patients Entered into the Self-Management Study

	% of All Entered Patients	% of Entered Patients Whose Asthma Is			$\chi^2$
		Mild	Moderate	Severe	
Medications recommended (N = 261)					
Inhaled bronchodilator	89.7	85.4	90.8	95.7	3.80
Continuous theophylline	87.4	75.0	94.1	95.7	21.06*
More than 1 course of steroids in past yr	41.2	20.0	45.4	73.9	36.82*
Another inhaled medication	36.8	26.0	42.9	43.5	7.53†
More than 1 course of antibiotics in past yr	27.6	29.2	23.5	34.8	2.29
Total No. of medications in recommended regimen (N = 261)					
0	1.1	3.1	0.0	0.0	41.13*
1	9.2	15.6	6.7	2.2	
2	31.8	44.8	26.1	19.6	
3	30.3	19.8	39.5	28.3	
4	19.2	12.5	19.3	32.6	
5	9.4	4.2	8.4	17.4	
Adherent to recommended regimen on all					
6 medication items	49.1	51.3	45.9	53.3	0.91
6 inhaler items	23.9	27.7	20.2	26.1	1.61
10 inhaler use items	13.1	8.0	13.8	22.5	5.09

\*p&lt;0.01.

†p&lt;0.05.

were common. Airflow obstruction was the most common symptom complex. There is a clear-cut increasing relationship with increasing severity for the symptom checklist scales, with the relationship more prominent for irritability and panic-fear.

The results in Table 5 indicate that patients experienced a variety of respiratory illnesses in the year prior to interview. Seventy-five percent of patients experienced episodes of shortness of breath, and only shortness of breath was related to increasing severity of asthma. Many patients experienced significant symptoms during the seven days prior to interview (a period short enough to be remembered accurately). Coughing, shortness of breath, and wheezing occurred with about equal frequency. All assessed symptoms, with the exception of increased sputum and green or yellow sputum, were more likely to occur in patients with more severe asthma.

Table 6 indicates that there was significant variability in the number of medications used by individual patients but most patients were taking two or three medications. Some patients were taking as many as five medications and a very small number, 1.5 percent with mild asthma, were receiving no medication at the time of data collection. In this asthma population, inhaled adrenergic agents were the most commonly used medications. Most patients took both theophylline and an inhaled adrenergic medication. A substantial proportion, about 35 percent, of patients received more than one course of steroids per year. About 32 percent used another inhaled medication, most often inhaled steroids. About 24 percent of patients received more than one course of antibiotics per year. Of the

standardly recommended medications, only continuous theophylline, more than one course of steroids, and use of another inhaled medication were related to severity. Continuous theophylline was seldom used in the treatment of the mild asthma.

The overall level of adherence in the UAB population was quite low, with less than half the patients

Table 7—Side Effects of Medication in Patients Entered into the Self-Management Study

Side Effects Experienced in Past 3 mo (N = 256)	% of All Entered Patients	% of Entered Patients Whose Asthma Is			$\chi^2$
		Mild	Moderate	Severe	
Tachycardia	46.9	35.3	52.9	52.2	6.91*
Insomnia	41.0	27.8	47.1	50.0	9.86*
Nausea	24.6	17.8	29.4	26.1	3.79
Bad dreams	10.2	8.9	10.1	13.0	0.56
Oral thrush	9.0	2.2	11.8	15.2	6.31*
Seizures	2.0	1.1	0.8	6.5	6.09*
Other	33.6	24.4	37.8	39.1	4.97

Relationship of Incidence of Side Effects to Type of Medication (N = 256)	Total No. of Side Effects in Past 3 mos for Those				t
	Not Taking Mean $\pm$ SD		Taking Mean $\pm$ SD		
Inhaled bronchodilator	1.44	1.97	1.69	1.43	0.85
Continuous theophylline	1.16	1.53	1.74	1.41	2.11*
More than 1 course of steroids	1.41	1.35	2.04	1.48	3.45†
Another inhaled medication	1.71	1.45	1.59	1.42	0.64
More than 1 course of antibiotics	1.57	1.36	1.90	1.55	1.59

\*p&lt;0.05.

†p&lt;0.01.

Table 8—Health Care Utilization in Patients Entered into the Self-Management Study (N = 257)\*

	% of All Entered Patients	% of Entered Patients Whose Asthma Is			$\chi^2$
		Mild	Moderate	Severe	
In the past year has					
Called a physician about a respiratory problem	43.2	37.6	41.5	58.7	5.81
Visited a physician for a respiratory problem	49.0	43.0	44.9	71.7	11.64†
Visited an emergency room for a respiratory problem	41.2	26.9	47.5	54.3	13.06†
Been hospitalized for a respiratory problem	27.6	16.1	28.8	47.8	15.62†
Visited emergency room or hospitalized	48.6	32.3	55.1	65.2	17.02†
Total No. of types of care used					
0	26.5	35.5	22.9	17.4	30.83†
1	21.8	21.5	27.1	8.7	
2	26.8	30.1	24.6	26.1	
3	14.0	9.7	15.3	19.6	
4	10.9	3.2	10.2	28.3	

\*Note: entries are percents of columns.

†p&lt;0.01.

adhering to the recommended medication regimen, less than 25 percent to the inhaler regimen, and only about one patient in six using inhalers correctly. These adherence levels were highly similar to those of other chronic adult diseases for which programs to improve self-management practices improved functional status and reduced overutilization of health care services.<sup>21</sup>

The information in Table 7 indicates that medication side effects were common, with 55 percent of patients experiencing tachycardia and 46 percent experiencing insomnia. Thirty-six percent of patients experienced some side effect other than those specifically listed on the questionnaire, and 28 percent experienced nausea. Tachycardia, insomnia, and bad dreams were more likely to occur in patients with severe asthma. On the other hand, "other" side effects were most likely to occur in patients with moderate asthma.

The impact of taking vs not taking each of the individual medications on side effects is also examined in Table 8. Although the side effect score was higher when individuals took any medicine, regardless of which medicine it was, only continuous theophylline and more than one course of steroids in the past year showed a statistically significant difference.

Table 8 summarizes the results for health care utilization. The absolute level of health care utilization was fairly high, with nearly half of the study patients having visited an emergency room, having been hospitalized, or having done both for a respiratory problem in the past year. All forms of health care, other than calling a physician about a respiratory problem, were used more by patients with more severe asthma.

#### DISCUSSION

Asthma is a very common disease, treated by a variety of physicians, including general internists, pediatricians, family practitioners, and other primary care providers. Many questions remain unanswered

about the current status of diagnostic accuracy and about the best treatment for asthma patients. This analysis of characteristics and correlates of asthma in a university clinic population is an important step in defining what is known and in indicating areas in which further asthma research is needed.

Previous epidemiologic data indicate that among children, boys are more likely to have asthma.<sup>16-18</sup> Although the National Institute of Allergy and Infectious Diseases (NIAID) task force concluded in 1979 that being male is a risk factor for asthma,<sup>11</sup> other reports suggest that asthma prevalence either does not differ between adult men and women<sup>14,15</sup> or that adult women predominate in clinic populations.<sup>12</sup> The predominance of female subjects in the UAB population confirms these latter results. There has been no satisfactory explanation of this apparent discrepancy between epidemiologic and clinical results. Several explanations are possible: (a) femaleness may really be a risk factor for asthma in adults, (b) female subjects may seek medical care more frequently than male subjects, or (c) diagnostic discrepancies are possible between the sexes, especially in older adults because it is difficult to distinguish airflow obstruction caused by asthma from that caused by chronic bronchitis and/or emphysema.<sup>22</sup> International Classification of Disease Code<sup>23</sup> lists many diagnostic possibilities for airflow obstruction, including nonspecific terms such as COPD, chronic bronchitis, bronchiolitis, etc. Therefore, the diagnosis of airflow obstruction is difficult and complex and could be influenced by diagnostic bias. Specifically, some investigators have suggested physicians tend to diagnose male subjects who smoke and wheeze as having COPD and female subjects with the same symptoms as having asthma.<sup>16</sup>

A broad age range of asthmatics has been noted,<sup>22</sup> extending from early childhood through late adulthood with peak ages of prevalence between 5 and 14 years

2023379580

and 50 to 70 years.<sup>18</sup> Previous spirometric studies have suggested an association between asthma and chronic airflow obstruction, with the loss of pulmonary function being greater in persons with more severe asthma.<sup>24</sup> Also, the "Dutch Hypothesis," which holds that among persons predisposed to asthma those who smoke are at the greatest risk of chronic obstruction,<sup>25</sup> has won increasing acceptance in recent years.

The data in Table 3 provide confirmation that a progressive decline in pulmonary function is associated with asthma of long duration. This decline has major implications for the natural history of asthma and provides circumstantial evidence for the clinical impression that asthma itself may be a risk factor for irreversible airway obstruction. The data in this table do not support the "Dutch Hypothesis," however, in that no relationship was found between smoking status and pulmonary function. This lack of relationship strengthens the evidence that the mere presence of asthma is the relevant risk factor for chronic obstruction.

Moreover, the data in Table 3 may underestimate the relationship between asthma duration and decline in pulmonary function. The data in Table 2 indicate that only 16.9 percent of the sample had received a diagnosis of asthma 30 or more years ago. This proportion is surprisingly small, and one possible explanation involves our decision to exclude all patients with chronic or disabling diseases. Over a period of 30 years or longer, the primary diagnosis for patients whose pulmonary function has declined progressively may have changed from asthma to COPD. Such patients would not have even been considered for the present study and thus would have reduced the number of long-duration asthma patients with severe obstruction. Alternative explanations can be proposed for the small proportion of long-duration patients, such as the possibility that many patients who received an asthma diagnosis many years ago are dead or the possibility that remission rate increases with asthma duration. The present data do not permit a decision among these possible explanations, and the implications of a relationship between asthma and irreversible airway obstruction are important enough to justify research directly addressing the issue.

We believe the Bother Scales will be valuable for future studies in education and behavioral research and in pharmacologic and immunologic research. Increased asthma symptomatology in the UAB population seems to be associated with fall and winter. Ragweed exposure is greatest during the fall in Birmingham, Ala. and the fall and winter are associated with increasing viral infections and increased exposure to fungal spores. Careful observation of immunologic phenomena during the fall may be required to understand this problem. It is somewhat surprising that we

did not observe greater variation among the seasons. Birmingham has a warm, moist climate, and greater seasonal variation might be observed in areas with longer, colder winters. Symptoms during the past seven days as well as the past 24 hours were more bothersome in patients with increasingly severe asthma.

The frequency with which respiratory symptoms occurred in the UAB asthma population confirms the difficulty of achieving a symptom-free state even under careful monitoring and treatment. The frequency of coughing as a symptom is important as it appears greater than would be expected from current literature.<sup>23</sup> Because asthma is a common diagnosis and cough is a common presenting symptom, these results suggest that assessment of pulmonary function, including measurement of flow rate and bronchial reactivity, should be considered in all patients who cough without any other obvious reason.

Medications typically prescribed for adults with asthma are those intended to prevent or reverse airflow obstruction. These medications vary from periodic use of inhaled adrenergics to multiple drug regimens, at times including systemic corticosteroids.<sup>26</sup> Theophylline and, to an even greater extent, steroids are the medications most likely to cause side effects. The relationship between the use of medications with side effects and severity of asthma raises important risk-benefit issues. Carefully controlled studies of the specific benefits and disadvantages of medication regimens need to be conducted to better define which patients should receive which regimen. Large prospective studies will most likely be required to answer these important therapeutic questions.

**ACKNOWLEDGMENTS:** The authors gratefully acknowledge the valuable contributions of the other members of the project staff: Beverly Martin, B.S., R.N.; Lydia Stewart, B.S.; William E. Goetter, M.D.; and Darlene Higgins, B.A.

#### REFERENCES

- 1 National Institute of Allergy and Infectious Disease (NIAID). Asthma and other allergic disease. Report of NIAID Task Force. Washington, DC: US Government Printing Office, 1979. NIH publication (PHS)79-387.
- 2 Evans R, Mullaly DI, Wilson RW, Gergen PJ, Rosenberg HM, Grauman JS, et al. National trends in the morbidity and mortality of asthma in the U.S.: prevalence, hospitalization and death from asthma over two decades: 1965-1994. *Chest* 1997; 91:65-745.
- 3 Burney P, Detels R, Higgins MI, Peckham C, Samet JM, Tager IB. Recommendations for research in the epidemiology of asthma. *Chest* 1987; 91:194-955.
- 4 Bailey WC, Richards JM, Manzella BA, Windsor RA, Brooks CM, Soong SJ. Promoting self-management in adults with asthma: an overview of the UAB program. *Health Educ Q* 1987; 24:345-55.
- 5 Bailey WC, Richards JM, Manzella BA, Windsor RA, Brooks CM, Soong SJ. Improving self-management skills of adults with asthma. *Am Rev Respir Dis* 1989; 139:144A.
- 6 Bailey WC, Soong SJ, Brooks CM, Windsor RA, Richards JM.

- Goetter WE. Demographics, co-morbidity, and medication in an asthma population. *Chest* 1987; 92:1225.
7. Richards JM, Bailey WC, Windsor RA, Martin B, Soong S. Some simple scales for use in asthma research. *J Asthma* 1988; 25:363-71.
8. Brooks CM, Richards JM, Bailey WC, Martin B, Windsor RA, Soong S. Subjective symptomatology of asthma in an outpatient population. *Psychosom Med* 1989; 51:102-08.
9. Manzella BA, Brooks CM, Richards JM, Windsor RA, Soong S, Bailey WC. Assessing the use of metered dose inhalers by adults with asthma. *J Asthma* 1989; 26:223-30.
10. Kinsman RA, Luparello T, O'Banion K, Spector S. Multidimensional analysis of the subjective symptomatology of asthma. *Psychosom Med* 1973; 35:250-67.
11. Morrissey DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care* 1986; 24:67-74.
12. Epstein SW, Manning CD, Ashley MJ, Correy PN. Survey of the clinical use of pressurized aerosol inhalers. *Can Med Assoc J* 1979; 120:813-16.
13. Pedersen PA, Weeke ER. Asthma in Danish general practice: prevalence and consultation. *Allergy* 1981; 36:175-81.
14. Brnder I, Higgins MW, Mathews KP, Keller JB. Epidemiology of asthma and allergic rhinitis in a total community, Tecumseh, Michigan. III: second survey of the community. *J Allergy Clin Immunol* 1974; 53:127-38.
15. Schachter EN, Doyle CA, Beck GJ. A prospective study of asthma in a rural community. *Chest* 1984; 85:623-30.
16. Tager IB, Weiss ST, Speizer FE. Occurrence of asthma, nonspecific bronchial hyperresponsiveness and atopy: insights from cross-sectional epidemiological studies. *Chest* 1987; 91:114-195.
17. Anderson HR, Bland JM, Peckham CS. Risk factors for asthma up to 16 years of age: evidence from a national cohort study. *Chest* 1987; 91:127-305.
18. Burrows B. The natural history of asthma. *J Allergy Clin Immunol* 1987; 80:373-775.
19. Jarvik ME, Cullen JW, Gritz ER, Voght TM, West LJ. Research on smoking behavior. Washington, DC: US Government Printing Office; 1977.
20. Shopland DR, Brown C. Changes in cigarette smoking prevalence in the U.S.: 1955 to 1983. *Ann Behav Med* 1985; 7:5-8.
21. Haynes R, Taylor D, Sackett D. Compliance in health care. Baltimore, Md: The Johns Hopkins University Press; 1979.
22. Dodge R, Cline MG, Burrows B. Comparisons of asthma, emphysema, and chronic bronchitis diagnosis in a general population sample. *Am Rev Respir Dis* 1986; 133:981-96.
23. International Classification of Disease, 9th Revision, Clinical Modification, vol 2. DHHS publication No. (PHS)80-1260. 1980.
24. Martin AJ, Landau LI, Phelan PD. Lung function in young adults who had asthma in childhood. *Am Rev Respir Dis* 1980; 122:609-16.
25. Orie NGM, Sluiter HJ, DeVries GA. The host factor in bronchitis. In: Orie NGM, Sluiter HJ, eds. *Bronchitis: an international symposium*. Assen:Royal Van Gorcum; 1961:43-59.
26. Bailey WC. Symposium on asthma. *Clin Chest Med* 1984; 5:555-56.

## Advanced Seminars in Diagnostic Imaging

The University of California, San Diego School of Medicine, will present this postgraduate course December 7-9 at the Ritz-Carlton Resort Hotel, Laguna Niguel, California. For information, contact: Dawne Ryals, Ryals & Associates, PO Box 1925, Roswell, Georgia 30077-1925 (404:641-9773).

2023379582

**H**

**2023379583**

**CONFOUNDERS**

**2023379584**

## CONFOUNDERS

Studies on parental smoking and childhood respiratory disease rarely address confounding variables. Confounding variables are factors that can create a "false" association between two elements by being associated with one or both of them. For example, factor X (socioeconomic status) may be associated with both factor Y (parental smoking) and factor Z (childhood respiratory disease). When factor X is not controlled for in epidemiological studies of the possible association between factor Y and factor Z, a false association may appear between factors Y and Z. Therefore, it is vital that epidemiologists control for confounding variables when conducting studies such as those on parental smoking. The possible confounding variables associated with parental smoking and childhood respiratory disease can be grouped into four major categories: (1) household heating and cooking sources; (2) outdoor air pollution; (3) organic substances; and (4) demographic, medical and socioeconomic factors.

2023379585



### Household heating and cooking sources

Children living in households with gas stoves have been reported to have a greater history of respiratory illness before the age of two and small but significantly lower levels of FEV<sub>1</sub> and FVC corrected for height<sup>1</sup> (FEV<sub>1</sub> and FVC are standard measurements of lung capacity and function). Similarly, exposure of children to gas cooking in the first two years of life has been associated with an increased risk of hospitalization for respiratory illness<sup>2</sup>. There are reported associations of gas stove use with daily peak flow in asthmatic, normal, and allergic subjects.<sup>3</sup>

Oxides of nitrogen (NO<sub>x</sub>) arising from the use of gas stoves for cooking were proposed to be related to a reported increase in cough, "colds going to the chest," and bronchitis in a study of 5,758 English and Scottish children aged six to eleven years<sup>4</sup>. A number of other confounders were controlled for in this study, including "age, social class, latitude, population density, family size, overcrowding, outdoor levels of smoke and sulphur dioxide and types of fuel used for heating." One group of researchers reported similar results for a five-year longitudinal study of 4827 boys and girls, ages five to ten years. This reported association was independent of age, sex, social class, number of cigarette smokers in the home, and latitude, and was only found in urban areas.<sup>5</sup>

2023379586

Use of unvented kerosene heaters, which release nitrogen dioxide ( $\text{NO}_2$ ) into the indoor environment, was associated with significantly more days of acute respiratory illness in exposed children<sup>6</sup>. In this study, there was no difference in the number of cigarettes smoked daily in the homes of exposed versus unexposed children.  $\text{NO}_2$  exposure was also reported to be associated with a risk of reporting lower respiratory symptoms in children under the age of seven<sup>7</sup>.

One study reported increased proportions of chest illnesses and hospitalizations for chest illness before age two in young children living in homes heated by wood-burning stoves. Medical histories, sociodemographic factors, or exposure to other pollutant sources did not account for the reported association<sup>8</sup>.

In another report, hot water heating systems were reported to have a large effect on lung function in children, when compared to the use of forced air heating and air conditioning systems<sup>9</sup>.

2023379587

## REFERENCES

1. Speizer, F., et al., "Respiratory Disease Rates and Pulmonary Function in Children Associated with NO<sub>2</sub> Exposure," American Review of Respiratory Disease, 121(1): 3-10, 1980.
2. Ekwo, E.E., et al., "Relationship of Parental Smoking and Gas Cooking to Respiratory Disease in Children," Chest 84(6): 662-668.
3. Lebowitz, M.D., "The Effects of Environmental Tobacco Smoke Exposure and Gas Stoves on Daily Peak Flow Rates in Asthmatic and Non-Asthmatic Families," ETS - Environmental Tobacco Smoke: Report from a Workshop on Effects and Exposure Levels, eds., R. Rylander, et al., European Journal of Respiratory Diseases Suppl., 133(65): 90-97, 1984.
4. Melia, R.J.W., et al., "Association Between Gas Cooking and Respiratory Disease in Children," British Medical Journal, 149-152, 1977.
5. Melia, R.J.W., et al., "The Relation Between Respiratory Illness in Primary Schoolchildren and the Use of Gas for Cooking, I - Results From a National Survey," International Journal of Epidemiology, 8(4): 333-338, 1979.

2023379588

6. Berglund, B., et al., "Radon, Passive Smoking, Particulates and Housing Epidemiology," Indoor Air 2: 255-260, 1984.
7. Berwick, M., et al., "Lower Respiratory Symptoms in Children Exposed to Nitrogen Dioxide From Unvented Combustion Sources," Environment International 15: 369-373, 1989.
8. Osborne, J.S. and R.E. Honicky, "Health Effects of Heating With Wood: Chest Illness in Young Children and Indoor Heating with Woodburning Stoves," The Human Equation: Health and Comfort, ASHRAE/SOEH Indoor Air Quality '89, April 17-20, 1989, San Diego, CA.
9. Hosein, H.R., et al., "The Effect of Domestic Factors on Respiratory Symptoms and FEV<sub>1</sub>," International Journal of Epidemiology 18(2): 390-396, 1987.

2023379589

### Outdoor air pollution

Outdoor air pollutants have been identified as a confounder in several studies. In one study, acute respiratory disease incidence was reported to be positively associated with higher ambient sulfate levels<sup>1</sup>.

A group of researchers examined the importance of indoor and outdoor environmental factors (parental smoking, gas cooking, suspended particulates and sulfur dioxide) in the respiratory health of seven- to ten-year-old Canadian children. The researchers were unable to identify any effects of parental smoking or gas cooking because the prevalence of these variables was highest in an industrial area of high particulate pollution<sup>2</sup>.

One researcher has reported a strong association between respiratory illness and particulate pollution in children living in a study site which experiences relatively high levels of particulate pollution<sup>3</sup>.

A study comparing Israeli children living in a polluted industrial town versus those living in an unpolluted area reported that chronic respiratory symptoms and most pulmonary diseases were significantly more common among those children from the polluted town<sup>4</sup>.

2023379590

## REFERENCES

1. Harrington, W. and Krupnick, Alan J., "Short-Term Nitrogen Dioxide Exposure and Acute Respiratory Disease in Children," JAPCA 35: 1061-1087, 1985.
2. Kerigan, A., et al., "A Three-Year Cohort Study of the Role of Environmental Factors in the Respiratory Health of children in Hamilton, Ontario," American Review of Respiratory Disease, 133: 987-993, 1986.
3. Pope, C., "Respiratory Disease Associated with Community Air Pollution and a Steel Mill, Utah Valley," AJPH, 79(5): 623-628, 1989.
4. Goren, A.I. and S. Hellmann, "Prevalence of Respiratory Symptoms and Diseases in Schoolchildren Living in a Polluted and in a Low Polluted Area in Israel," Environmental Research 45: 28-37, 1987.

2023379591

## Organic substances

The relevance of home dampness in the etiology of respiratory symptoms in children is supported by current research which links dampness with the presence of molds, dust mites, fungi and other allergenic microbes.

In one study, odds ratios of 1.23 and 2.16 were reported for home dampness after adjustment for several factors, including maternal smoking, in a cohort study of 4,625 eight- to twelve-year-old children living in six United States cities<sup>1</sup>. The authors reported odds ratios for molds of 1.27 to 2.12 after adjustment for maternal smoking and several other factors.

Another study reported higher rates of respiratory symptoms and symptoms of infection and stress among children living in damp houses. The presence of "fungal mould" was also reported to be related to higher rates of respiratory symptoms, independent of smoking in the household<sup>2</sup>. In another study, the growth of fungi and molds in the home was directly related to respiratory symptoms and sensitization to common allergens in children<sup>3</sup>.

Researchers have reported that children living in damp and moldy dwellings had a greater prevalence of respiratory symptoms and headache and fever than those living in dry homes. The authors reported a dose-response relationship with increasing

2023379592

numbers of symptoms reported in dwellings with higher severity of dampness and mold. All these differences persisted after controlling for possible confounding factors such as household income, cigarette smoking, unemployment, and overcrowding<sup>4</sup>.

Atopic sensitization of children to house dust mites was reported to be related to home dampness<sup>5</sup>.

2023379593



## REFERENCES

1. Brunekreef, B., et al., "Home Dampness and Respiratory Morbidity in Children," American Review of Respiratory Diseases 140: 1363-1367, 1989.
2. Martin, C., et al., "Housing Conditions and Ill Health," British Medical Journal, 294: 1987.
3. Ownby, D. and J. McCullough, "Passive Exposure to Cigarette Smoke Does Not Increase Allergic Sensitization in Children," J Allergy Clin Immunol 82(4): 634-638, 1988.
4. Platt, S., et al., "Damp Housing, Mould Growth, and Symptomatic Health State," British Medical Journal, 298: 1673-1678, 1989.
5. Nordvall, S.L., et al., "Sensitization of Children in the Stockholm Area to House Dust Mites," Acta Paediatr Scan, 77(5): 716-720, 1988.

2023379594

### Demographic, medical and socioeconomic factors

Low socioeconomic status has been associated with an increased incidence of respiratory complications<sup>1</sup>. Factors related to lower socioeconomic status include: inadequate medical care, poor nutrition, poor outdoor air quality, increased parental coughing, higher gas stove usage, frequent change of address, and lower per capita living space. In a study of 1,050 European children aged eight and nine years, lifetime and current prevalence of wheeze were both significantly higher in children from low socioeconomic status<sup>2</sup>.

Watkins, et al., (1986) reported high consultation rates for respiratory illness in children whose fathers were in manual occupations. This association was not explained by crowded home conditions or parental smoking<sup>3</sup>. Gardner, et al., (1984) reported significantly higher rates of lower respiratory disease in infants of low socioeconomic status<sup>4</sup>.

Cross-infection also plays a role in the incidence of children's respiratory disease. For instance, in a 1988 paper, Koo, et al., reported that among Japanese and Hong Kong Chinese women, there was a highly significant correlation between the frequency of maternal respiratory illness and the frequency of respiratory illness in her children<sup>5</sup>.

2023379595

Cross-infection may be relevant to the reports of associations between day care attendance and respiratory illness. Anderson, et al., (1988) reported that care outside the home (day care) is an important factor for acquiring lower respiratory tract illness and infectious diseases in children under two years of age<sup>6</sup>. Gardner, et al., (1984) also noted significantly higher rates of lower respiratory disease among day care infants<sup>4</sup>. Fleming, et al., (1987) reported an increased risk for upper respiratory tract infection associated with day care attendance<sup>7</sup>.

Familial characteristics and genetics may also act as confounders. For instance, in a 1982 publication, Lebowitz, et al., report that an observed relationship between children's pulmonary function and parental smoking disappeared when household aggregation of body mass was taken into account<sup>8</sup>. Another Lebowitz, et al., study (1984) also reported that there was "no remaining independent aggregation of pulmonary function measurements" after familial aggregation of body habitus was controlled for<sup>9</sup>. Genetic predisposition may play a role in respiratory illness and pulmonary function<sup>10</sup>; although cross-infection is also involved<sup>11</sup>.

"Lifestyle" may also act as a confounder. A study in Copenhagen (Holma and Winding, 1977) examined 109 social, medical, housing, and hygiene factors on morbidity. The best predictors for health were "thriving" (satisfaction), followed by "housing standard" and "personal hygiene." The authors reported no effect

2023379596

of parental cigarette smoking on the respiratory health of young children<sup>12</sup>. A survey of 314 nonsmoking Hong Kong Chinese women and their children and 243 Japanese women and their children reported that chronic cough and sputum symptoms were at least 10 times more prevalent in Hong Kong<sup>5</sup>. This observation was attributed to occupational exposure to dust or fumes and household crowding among the Hong Kong mothers.

2023379597

## REFERENCES

1. Kerigan, A., et al., "A Three-Year Cohort Study of the Role of Environmental Factors in the Respiratory Health of Children in Hamilton, Ontario," American Review of Respiratory Diseases, 133: 987-993, 1986.
2. Mitchell, E., et al., "Socioeconomic Status in Childhood Asthma," International Journal of Epidemiology, 18(4): 888-890, 1989.
3. Watkins, C.J., et al., "Patterns of Respiratory Illness in the First Year of Life," British Medical Journal, 293: 794-796, 1986.
4. Gardner, G., et al., "Effects of Social and Family Factors on Viral Respiratory Infection and Illness in the First Year of Life," Journal of Epidemiology and Community Health 38(1): 42-48, 1984.
5. Koo, L., et al., "A Comparison of the Prevalence of Respiratory Illness Among Nonsmoking Mothers and Their Children in Japan and Hong Kong," Respiratory Illnesses Among Japanese and Chinese Mothers and Their Children: 290-295, 1988.

2023379598

6. Anderson, L., et al., "Day Care Center Attendance and Hospitalization for Lower Respiratory Tract Illness," Pediatrics 82(3): 300-308, 1988.
7. Fleming, D.W., et al., "Childhood Upper Respiratory Tract infections: To What Degree Is Incidence Affected by Day-Care Attendance?" Pediatrics 79(1): 55-60, 1987.
8. Lebowitz, M., et al., "The Effect of Passive Smoking on Pulmonary Function in Children," Environment International, 8: 371-373, 1982.
9. Lebowitz, M., et al., "Family Aggregation of Pulmonary Function Measurements," American Review of Respiratory Diseases, 129: 8-11, 1984.
10. Colley, J.R.T., et al., "Influence of Passive Smoking and Parental Phlegm on Pneumonia and Bronchitis in Early Childhood," The Lancet II: 1031-1034, 1974.
11. Colley, J.R.T., "Respiratory Symptoms in Children and Parental Smoking and Phlegm Production," British Medical Journal 2: 201-204, 1974.

2023379599

12. Holma, B. and Winding, O., "Housing, Hygiene, and Health: A Study in Old Residential Areas in Copenhagen," Archives of Environmental Health 32(2): 86-93, 1977.

2023379600

PARENTAL SMOKING: CONFOUNDING VARIABLES

Access to medical care  
Age of mother  
Air pollution  
Birth weight  
Breast feeding  
Cooking practices/type  
Day care attendance  
Diet  
Family history of illness  
Family size  
Gender of child  
Genetic determinants  
Heating type  
Home dampness  
Hospital spread of illness  
Household pets  
Newborn illnesses  
Nurture  
Overcrowding  
Parental education  
Parental infections  
Place of residence  
Seasonal variation  
Skin test reactivity (allergy)  
Socioeconomic status

2023379601



**2023379602**

Colley, J.R.T. "Respiratory Symptoms in Children and Parental Smoking and Phlegm Production" British Medical Journal 2: 201-204, 1974.

SUMMARY: A study of respiratory symptoms in 2,426 school children aged 6-14 years was carried out in Aylesbury, Buckinghamshire, in 1971. The prevalence of cough in the children was associated with the parents' smoking habits; prevalence was lowest where both parents were non-smokers, highest where both parents smoked, and lay between these two levels where only one parent smoked. A close association was found between parents' and childrens' respiratory symptoms that was independent of parents' smoking habits. There was no suggestion that exposure to the cigarette smoke generated when parents smoked had any more than a small effect upon the child's respiratory symptoms. While the sharing of genetic susceptibility between parents and children is a factor, therefore, cross infection, particularly in the families where parents smoke, is an important element in the association.

2023379603

## Discussion

Despite the increase in our knowledge and understanding of the pathogenic mechanisms present in patients with diffuse toxic goitre—particularly since the discovery of LATS (Adams, 1958) and its characterization as an immunoglobulin (Adams and Kennedy, 1962; McKenzie, 1962; Kriss *et al.*, 1964; Dorrington *et al.*, 1966)—the cause of the abnormal thyroid function in this disease has remained uncertain. The simplest explanation, and the only one which accounts for the phenomenon of neonatal thyrotoxicosis, is that there is a circulating humoral stimulator acting upon the gland (McKenzie, 1972). Thyrotrophin has been excluded from this role by the fact that its level in blood is less than normal in diffuse toxic goitre (Adams *et al.*, 1969). To many workers LATS has been unacceptable as a causative agent because it is undetectable in many cases and the level in any individual patient does not correlate with the degree of abnormal thyroid function (Volpe *et al.*, 1972). LATS protector, however, meets two criteria not fulfilled by LATS; our evidence confirms the high incidence of LATS protector in diffuse toxic goitre and shows that its serum level correlates well with early thyroid <sup>131</sup>I uptake. Furthermore, LATS protector has been shown to stimulate the human thyroid, both *in vitro* (Shishiba *et al.*, 1973) and *in vivo* (Adams *et al.*, 1974). We therefore think that in LATS-negative patients with diffuse toxic goitre LATS protector is the pathogenic agent.

The question whether LATS protector is present in every case of diffuse toxic goitre remains open. It was not found in five of the 50 patients studied, but all these were relatively mild cases with normal or only slightly raised thyroid <sup>131</sup>I uptake and large goitres. Failure to detect LATS protector in these inactive cases may have been due to assay insensitivity, but incorrect diagnosis of thyrotoxicosis or an alternative pathogenic mechanism for thyroid dysfunction are other possible explanations.

The pathogenesis of the ophthalmopathy of Graves's disease remains less well understood than the pathogenesis of thyrotoxicosis. We found no significant correlation between the class of ophthalmopathy and the LATS protector level. The highest incidence of infiltrative ophthalmopathy, however, was observed in the group of patients with both LATS and LATS protector, and the lowest incidence was in those patients in whom neither immunoglobulin could be detected. Our findings support the view that LATS protector and ophthalmopathy may be associated in Graves's disease but the relation is not a causal one.

We thank Mr. W. S. Cague for skilled technical help.

Requests for reprints should be addressed to Dr. R. D. H. Stewart.

## References

- Adams, D. D. (1958). *Journal of Clinical Endocrinology and Metabolism*, 18, 699.
- Adams, D. D., *et al.* (1974). *Journal of Clinical Endocrinology and Metabolism*, in press.
- Adams, D. D., and Kennedy, T. H. (1962). *Proceedings of the University of Otago Medical School*, 40, 6.
- Adams, D. D., and Kennedy, T. H. (1967). *Journal of Clinical Endocrinology and Metabolism*, 27, 173.
- Adams, D. D., and Kennedy, T. H. (1971). *Journal of Clinical Endocrinology and Metabolism*, 33, 47.
- Adams, D. D., Kennedy, T. H., and Purves, H. D. (1969). *Journal of Clinical Endocrinology and Metabolism*, 29, 900.
- Clark, F., and Horn, D. B. (1965). *Journal of Clinical Endocrinology and Metabolism*, 25, 39.
- Dorrington, K. J., Carneiro, L., and Munro, D. S. (1966). *Biochemical Journal*, 93, 858.
- Kriss, J. P., Pleshakov, V., and Chien, J. R. (1964). *Journal of Clinical Endocrinology and Metabolism*, 24, 1005.
- McKenzie, J. M. (1962). *Journal of Biological Chemistry*, 237, 3571.
- McKenzie, J. M. (1972). *Metabolism*, 21, 883.
- Oddie, T. H., Meschan, I., and Wortham, J. (1955). *Journal of Clinical Investigation*, 34, 106.
- Shishiba, Y., Shimizu, T., Yoshimura, S., and Shirume, K. (1973). *Journal of Clinical Endocrinology and Metabolism*, 36, 517.
- Volpe, R., Edmunds, M., Lamki, L., Clarke, P. V., and Row, V. V. (1972). *Mayo Clinic Proceedings*, 47, 824.
- Werner, S. C. (1969). *Journal of Clinical Endocrinology and Metabolism*, 29, 942.

# Respiratory Symptoms in Children and Parental Smoking and Phlegm Production

J. R. T. COLLEY

*British Medical Journal*, 1974, 2, 201-204

## Summary

A study of respiratory symptoms in 2,426 schoolchildren aged 6-14 years was carried out in Aylesbury, Buckinghamshire, in 1971. The prevalence of cough in the children was associated with the parents' smoking habits; prevalence was lowest where both parents were non-smokers, highest where both parents smoked, and lay between these two levels where only one parent smoked. A close association was found between parents' and children's respiratory symptoms that was independent of parents' smoking habits. There was no suggestion that exposure to the cigarette smoke generated when parents smoked had any more than a small effect upon the child's respiratory symptoms. While the sharing of genetic susceptibility between parents and children is a factor, therefore, cross infection, particularly in the families where parents smoke, is an important element in the association.

## Introduction

Norman-Taylor and Dickinson (1972) suggested that children with parents who smoke may be at particular risk from respiratory disease. These authors were not, however, explicit about the nature of the risk. They implied that exposure of children to cigarette smoke at home might increase the risk of respiratory illness. This paper reports the findings of a study in which the nature of the association between parental smoking and respiratory disease in their children was investigated.

## Methods

The material was collected during a study of the prevalence of respiratory disease in schoolchildren and their parents in Aylesbury, Buckinghamshire, in 1971. The population consisted of all children aged 6-14 years attending seven schools in Aylesbury—a total of 2,598 children (1,328 boys and 1,270 girls). Data were collected on 2,426 children and their parents, a response rate of 93.4%.

A self-administered questionnaire was completed by the parents, who answered questions about their own and their

Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine, London WC1E 7HT.  
J. R. T. COLLEY, M.D., M.P.C.M., Senior Lecturer in Epidemiology

children's health. The relevant questions were: (a) for each child, Does he/she usually cough during the day or at night in the winter?; (b) for each parent, (1) Do you usually bring up any phlegm from your chest first thing in the morning in winter?; (2 a) Do you smoke? If "No"; (2 b) Have you ever smoked as much as one cigarette a day for as long as a year? Parents who answered "Yes" to question (2 a) were classified as smokers. They were also asked how many cigarettes they smoked a day, how many ounces of tobacco they smoked each week, and how many cigars, large and small, they smoked each week. Those parents that answered "No" to question (2 a) and answered question (2 b) in the negative were classified as non-smokers, while those that responded in the affirmative to question (2 b) were classified as ex-smokers. The validity of the question on cough in the children when used in a self-administered questionnaire has already been established (Colley and Reid, 1970), as has that of the question on phlegm production (Krueger *et al.*, 1970).

The father was asked about his occupation and from this his social class was obtained. (*Classification of Occupation*, 1970). The number of siblings which the index child had was also recorded.

## Results

The relation in the parents between smoking habits and prevalence of phlegm was what one would have expected; prevalence rose with amount smoked. Parents were classified by smoking habit into five groups; group 1, both parents non-smokers; group 2, one parent a smoker, the other a non-smoker; group 3, both parents smokers; group 4, both parents ex-smokers or one an ex-smoker and the other a non-smoker or smoker; and group 5, one or both parents gave no data on smoking habits. Within these five groups the prevalence in the children of cough during the day or at night in the winter was determined (table I). The cough prevalence rates were lowest

in children with one or both parents ex-smokers. The gradient in prevalence over groups 1, 2, and 3 was statistically significant ( $\chi^2$  for trend 6.865;  $0.01 > P > 0.005$ ). The findings indicated an association between parental smoking habits and the prevalence of symptoms in their children.

The analysis was taken a stage further by classifying parents by both smoking habits and by their response to the question, Do you usually bring up any phlegm from your chest first thing in the morning in winter? (table II). Within each group the prevalence of cough in children was lowest among children of parents who did not report symptoms. It was highest in those children where both parents reported symptoms. Where only one parent reported the symptom the prevalence rate lay between these two extremes. Overall, there was a threefold difference in prevalence of cough between children with neither parent having the symptoms and both having the symptom.

Some of the prevalence rates in table II were based on small numbers, but the numbers in the category where neither parent had symptoms allowed a firmer conclusion. It was thus interesting to note that in this category the prevalence of cough rose from 12.4% in children of non-smoking parents to 14.3% where one parent smoked and to 14.7% where both smoked. This trend while small and not statistically significant nevertheless raised the possibility that exposure to cigarette smoke at home when parents smoked might have had some effect on the child's respiratory tract. A more precise estimate of the effects of "passive smoking" by the child was obtained by estimating the maximum daily exposure of the child to their parents' cigarette smoke. This was derived by the addition of both parents' daily cigarette consumption. Among the children of parents who did not have morning phlegm there was a small gradient for cough prevalence according to the number of cigarettes (or tobacco equivalent) smoked by the parents (table III). This gradient in prevalence is not, however, statistically significant ( $\chi^2$  trend 1.36;  $0.30 > P > 0.20$ ).

TABLE I—Prevalence of Cough during Day or at Night in Winter in Children aged 6-14 according to Parents' Smoking Habits

	Parents' Smoking Group*					Total†
	1	2	3	4	5	
Percentage (No.) of children with cough	15.6 (320)	17.7 (547)	22.2 (634)	14.2 (620)	20.7 (217)	18.0 (2,338)

\*See text for composition of groups.

†Total excludes 88 children for whom there were no data on cough.

TABLE II—Prevalence of Cough during Day or at Night in Winter in Children aged 6-14 according to Parents' Smoking Habits and Presence of Winter Morning Phlegm

	Group 1			Group 2			Group 3			Group 4			Total*		
	Neither	One	Both	Neither	One	Both	Neither	One	Both	Neither	One	Both	Neither	One	Both
Winter morning phlegm in parents	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Percentage (No.) of children with cough	12.4 (274)	27.5 (40)	40.0 (5)	14.3 (420)	24.7 (97)	52.9 (17)	14.7 (369)	24.1 (159)	43.5 (69)	12.6 (499)	19.4 (98)	23.1 (13)	13.5 (1,582)	25.1 (394)	44.2 (104)

\*Total excludes 346 children for whom there were no data on cough or parents' smoking habits or morning phlegm.

TABLE III—Prevalence of Cough during Day or at Night in Winter in Children aged 6-14 according to Parents' Smoking Habits, Number of Cigarettes smoked, and Presence of Winter Morning Phlegm

	Group 1		Groups 2 and 3								Group 4		Total†	
			Total No. of Cigarettes*											
			1-9		10-19		20-29		>30					
Winter morning phlegm in parents	N	O/B	N	O/B	N	O/B	N	O/B	N	O/B	N	O/B	N	O/B
Percentage (No.) of children with cough	12.4 (274)	33.3 (45)	13.3 (135)	32.1 (28)	18.8 (247)	21.5 (65)	14.0 (208)	37.8 (74)	15.0 (208)	32.2 (174)	12.6 (499)	19.8 (111)	13.56 (1,571)	29.97 (497)

N=Neither, O/B=One or both.

\*Including tobacco and cigars expressed as cigarette equivalents (see Todd, 1972).

†Total excludes 358 children for whom there were no data on cough or parents' smoking habits or morning phlegm.

2023379605

Several points have to be considered in interpreting these findings. As in other studies (Holland *et al.*, 1969; Colley and Reid, 1970), social class gradients for respiratory symptoms in children were found in this series. Children with fathers in semi-skilled and unskilled occupations had higher prevalence rates for respiratory symptoms than those whose fathers were in skilled or non-manual occupations. A concentration of low social class families in the groups where both parents reported winter morning phlegm could have produced a similar pattern to that shown in table II. That this could not have accounted for the observed patterns of cough prevalence in the children may be seen in table IV, where cough prevalence is given for children in social class III according to the parents' history of phlegm production after standardization for smoking. Cough prevalence in the children increased, as before, with the presence of parental phlegm production.

TABLE IV—Prevalence in Social Class III of Cough during Day or at Night in Winter in Children aged 6-14 according to Parents' Phlegm (Standardized for Parents' Smoking Habits)

Parents with winter morning phlegm ..	Neither	One	Both
Percentage (No.) of children with cough ..	15.4 (824)	27.4 (207)	32.9 (54)

Children from large families have higher prevalence rates for respiratory symptoms than those from small families (Colley, 1970), and a concentration of large families in the groups of parents with symptoms might also have resulted in the prevalence of morning cough being similar to that shown in table II. It can be seen from table V, however, that within families of similar size the same gradients for cough prevalence according to parents' phlegm production were present, indicating that differences in the number of siblings could not have explained the gradient in cough prevalence.

TABLE V—Prevalence of Cough during Day or at Night in Winter in Children aged 6-14 according to Parents' Phlegm and Number of Siblings (Standardized for Parents' Smoking Habits)

Parents with Winter Morning Phlegm	No. of Siblings					
	Nil or 1		2		3 or More	
	No. of Children	Prevalence (%)	No. of Children	Prevalence (%)	No. of Children	Prevalence (%)
Neither	672	14.2	444	11.6	484	14.8
One	122	16.5	137	28.6	131	29.4
Both	25	37.9	27	37.5	52	44.4

Table excludes 348 children owing to lack of data on cough, or on parents' smoking habits or morning phlegm, or on family size.

Younger school children tend to have higher prevalence rates for winter cough than older children (Colley and Reid, 1970). If the age distributions of children in the various groups in table II had not been the same prevalence rates between these groups might also have differed, but there were no differences in age structure between these groups of children.

Conclusions drawn from the evidence in this study need to be viewed with caution because it was not possible to collect evidence which would have excluded some other interpretation of the results. It was possible, for example, that the parents' account of their own symptoms might have influenced the answers they gave for their children and that the apparent association between parents and children in their respiratory experience could have been due to parents with symptoms over-reporting symptoms in their children. The children of parents who smoked may also have been more likely to have smoked than children of non-smoking parents, and this could have resulted in an increased prevalence of cough in such children. If either of these possibilities had oc-

curred to any material extent it would have meant that, as given in table II the prevalence of cough in children from group 2 was too high in relation to cough in children from group 1 and that the prevalence of cough in children from group 3 was still higher. If the prevalence of cough in children from group 2 were to be reduced in order to correct for this and that of children from group 3 were to be corrected even more then the gradient shown in table II would probably become negative in that cough prevalence in children would have seemed to decline as more parents smoked. It therefore seems reasonable to conclude that the two possible qualifications to the data did not operate.

## Discussion

Norman-Taylor and Dickinson (1972) in their study of children's respiratory infections and parental smoking habits reported higher prevalence rates for various indices of respiratory disease among children with parents who smoke. The present study, using a single index of respiratory disease, confirms their findings. It can now be seen, however, that a direct association exists between respiratory symptoms in parents and in their children. Parental smoking has a mainly indirect effect on the child by increasing the prevalence of the parents' respiratory symptoms and thus the prevalence of respiratory symptoms in their children. The direct effect on the children's respiratory symptoms of exposure to the smoke generated when their parents smoked cigarettes seemed to be relatively small.

The reason for the association between respiratory symptoms in parent and child is not clear. The sharing of genetic susceptibility between parents and children could have led to these similarities in respiratory disease, but this is unlikely to be the whole explanation, particularly in families where both parents smoke. There is, for example, no convincing evidence that adults who take up smoking have a greater genetic susceptibility to respiratory disease than non-smokers, and therefore there is no reason to suppose that susceptibility to respiratory disease would be different in the children of smokers and non-smokers. On the other hand, smoking parents differed from the non-smokers in that they had higher prevalence rates for respiratory symptoms and the rates rose with the amount smoked, indicating some direct effect of smoking in causing their symptoms. In these circumstances the association between parents' and children's symptoms are more likely to be due to cross infection than to the sharing of genetic susceptibility.

If cross infection is indeed an important cause of respiratory symptoms in children of parents who smoke then there could well be some advantages for their children if the parents gave up the habit. In adults giving up smoking can result in a reduction in cough and expectoration and, therefore, in the chance of transmitting respiratory infections. Smoking parents, many of whom will not yet have developed severe or irreversible respiratory damage, can reasonably expect an improvement in symptoms if they give up the habit, and this would offer a promising way of reducing the risk of their children developing respiratory symptoms.

The findings in this paper need confirmation. This could be done by prevalence studies on a larger scale in other populations where, for example such aspects as the possible over-reporting of symptoms could be adequately investigated. There is a need to investigate the likely benefit to the child from parents giving up smoking. Though passive inhalation of cigarette smoke by the child has not been shown to have an important effect in this series, this aspect should nevertheless be studied in infants and preschool children, who tend to be the most susceptible to respiratory infections.

I thank Dr. J. J. A. Reid, who at the time of this study was County Medical Officer of Health, Buckinghamshire; Dr. A. W. Pringle, Aylesbury Area Medical Officer and Divisional School Medical Officer; the Buckinghamshire Education Department and the head teachers of the schools involved for their co-operation and help in this survey; Mrs. B. Hunt for the analysis of the data; Professor D. D. Reid who gave helpful advice in the preparation of this paper; and the field workers who included Mrs. B. Hunt, Miss S. J. Newby, S.R.N., Mrs. M. Pant, S.R.N., Miss J. P. E. Stocks, S.R.N., and Miss J. V. Tudhope, S.R.N.

#### References

- Classification of Occupations* (1970). (1972). Office of Population Censuses and Surveys, London, H.M.S.O.  
 Colley, J. R. T. (1970). *Proceedings of the Third International Symposium on Hemachia*, ed. N. G. M. Orie and R. van der Lende, p. 8. Assen, Netherlands, Royal Van Gorcum.  
 Colley, J. R. T., and Reid, D. D. (1970). *British Medical Journal*, 2, 213.  
 Holland, W. W., Hahl, T., Bennett, A. E., and Elliott, A. (1969). *Alibank Memorial Fund Quarterly*, 47, 215.  
 Krueger, D. F., Kocot, E., Blackwelder, W. C., and Reid, D. D. (1970). *Journal of Chronic Diseases*, 23, 411.  
 Norman-Taylor, W., and Dickinson, V. A. (1972). *Community Medicine*, 124, 32.  
 Todd, G. F. (1972). *Statistics of Smoking in the U.K.*, 6th edn., London Tobacco Research Council.

## Choreo-athetosis and Encephalopathy Induced by Phenytoin

D. L. McLELLAN, M. SWASH

*British Medical Journal*, 1974, 2, 204-205

### Summary

Two patients with intractable epilepsy who had been treated with various combinations of anticonvulsant drugs developed phenytoin encephalopathy. In both patients choreo-athetoid involuntary movements were prominent. Blood phenytoin concentrations were above 30 µg/ml. When phenytoin was given in smaller doses and its level in the blood fell the involuntary movements and other clinical manifestations disappeared.

### Introduction

Nystagmus, ataxia, dizziness, and drowsiness are well-known features of phenytoin toxicity which usually occur when the blood level is greater than 20 µg/ml (Buchthal *et al.*, 1960). There have been few reports of other toxic effects on the central nervous system though Glaser (1973) pointed out that a reversible encephalopathy may occur in some patients treated with large doses of the drug. We describe two patients in whom choreo-athetoid involuntary movements were a prominent and presenting feature and in whom the involuntary movements and the encephalopathy were closely correlated with very high blood phenytoin concentrations.

### Case Reports

#### CASE 1

A 31-year-old man who had attended hospital for many years for management of epilepsy was admitted for investigation of involuntary movements and intractable seizures. He had had a febrile convulsion when 2 years old and had had recurrent petit mal and major generalized seizures since he was 7. An electroencephalogram when he was aged 13 showed typical, generalized, three-per-second spike-and-wave complexes and diffuse bursts of theta and delta activity. When assessed for industrial training when aged 21 he had an I.Q. of 84 on the Wechsler Intelligence Scale. He was treated with various combinations of anticonvulsants,

including troxidone, ethosuximide, primidone, and phenytoin, but he continued to have two or three major seizures a month. When he was aged 29 Hodgkin's disease was diagnosed by biopsy of an enlarged cervical lymph node. No involvement of liver, spleen, or para-aortic nodes was seen on laparotomy and he was treated with radiotherapy to the neck. There had been no recurrence. Treatment with phenytoin 300 mg, phenobarbitone 150 mg, and ethosuximide 750 mg daily was continued. Two years later the seizures became more frequent (two to four a week) and primidone 750 mg, carbamazepine 800 mg, and phenytoin 450 mg daily were gradually substituted for the previous treatment. During the next six weeks he complained of blurred vision and ataxia, leading to frequent falls. He continued to take the drugs. The seizures continued unchanged.

On admission to hospital he was slightly drowsy but orientated. Several minor seizures were observed. He had grade I nystagmus in all directions and upward conjugate gaze was impaired. There was generalized chorea which was present at rest and was enhanced by movement, particularly by walking. Slurred and hesitant speech seemed to be due to interposed choreic movements of the lips and tongue. In the outstretched upper limbs choreiform involuntary movements were accompanied by irregular postural lapses of the fingers, which were thought to be typical of asterixis rather than chorea. The gait was unsteady, but there were no cerebellar signs in the limbs. There was no weakness or sensory impairment, the tendon reflexes were brisk, and both plantar responses were flexor. Hyperplasia of the gums was noted. The increased frequency of seizures and the encephalopathy with involuntary movements were first ascribed to a degenerative or infective disorder associated with the Hodgkin's disease. The haemoglobin, white cell count, E.S.R., liver function tests, blood urea and electrolytes, skull and chest x-ray examinations, and brain scan were normal. The background activity in the E.E.G. was fragmented and slowed and there was an excess of diffuse, irregular delta activity of moderate voltage. Generalized atypical spike-and-wave activity was prominent. The blood phenytoin concentration was 37 µg/ml.

The possibility of phenytoin encephalopathy was considered. The daily dose of phenytoin was reduced to 200 mg daily and that of primidone increased to 1 g. Carbamazepine 800 mg daily was continued. During the next six days the patient became more alert, the chorea, ataxia, and nystagmus disappeared, and the blood phenytoin level fell to 16 µg/ml. The seizures at first increased in frequency but then abated. Three weeks later he returned to work. Neurological findings at that time were normal.

#### CASE 2

This 15-year-old boy was referred for management of uncontrolled epilepsy. He had had frequent minor and major seizures since the age of 2 when he had presented in status epilepticus. He had been treated with varying combinations of phenytoin, phenobarbitone, ethosuximide, and sulthame and had been almost free

Department of Neurology, Section of Neurological Sciences, London Hospital, London E1 1BB

D. L. McLELLAN, M.B., M.R.C.P., Senior Registrar  
 M. SWASH, M.B., M.R.C.P., Consultant Neurologist

2023379608

Colley, J.R.T., Holland, W.W., Corkhill, R.T. "Influence of Passive Smoking and Parental Phlegm on Pneumonia and Bronchitis in Early Childhood" The Lancet (November 2): 1031-1034, 1974.

SUMMARY: The incidence of pneumonia and bronchitis has been studied in 2205 infants over the first five years of life. In the same period their parents' smoking habits and respiratory symptoms were recorded annually. The incidence of pneumonia and bronchitis in the first year of life was associated with parents' smoking habits; incidence was lowest where both parents were non-smokers, highest where both smoked, and lay between these two levels where only one parent smoked. Over the age of one year the association was not consistent. When parents' respiratory symptoms were also studied a close association was found with the incidence of pneumonia and bronchitis in the child; this was independent of parents' smoking habits and was an almost consistent finding throughout the first five years of life. In the first year of life exposure to cigarette smoke generated when parents smoked doubled the risk for the infant of an attack of pneumonia or bronchitis.

2023379609



# INFLUENCE OF PASSIVE SMOKING AND PARENTAL PHLEGM ON PNEUMONIA AND BRONCHITIS IN EARLY CHILDHOOD

J. R. T. COLLEY

*Department of Medical Statistics and Epidemiology,  
London School of Hygiene and Tropical Medicine,  
London WC1E 7HT*

W. W. HOLLAND

R. T. CORKHILL

*Department of Community Medicine, St. Thomas's  
Hospital Medical School, London SE1 7EH*

**Summary** The incidence of pneumonia and bronchitis has been studied in 2205 infants over the first five years of life. In the same period their parents' smoking habits and respiratory symptoms were recorded annually. The incidence of pneumonia and bronchitis in the first year of life was associated with parents' smoking habits; incidence was lowest where both parents were non-smokers, highest where both smoked, and lay between these two levels where only one parent smoked. Over the age of one year the association was not consistent. When parents' respiratory symptoms were also studied a close association was found with the incidence of pneumonia and bronchitis in the child; this was independent of parents' smoking habits and was an almost consistent finding throughout the first five years of life. In the first year of life exposure to cigarette smoke generated when parents smoked doubled the risk for the infant of an attack of pneumonia or bronchitis.

## Introduction

INFANTS who inhale the tobacco smoke generated when their parents smoke at home may have a greater risk of chest illness than the infants of non-smoking parents. We have studied the influence of parental smoking and respiratory symptoms for effects on the incidence of pneumonia and bronchitis in their children during the first five years of life.

## Methods

The data that form the basis of this paper are part of those collected during a longitudinal study of newborn infants and their families. The study was conducted in Harrow, a borough in north-west London, between 1963 and 1969 and involved all families living in six of the wards of the borough who had an infant born in the period

July 1, 1963, to June 30, 1965. A total of 2365 families had newborn infants during this period, and, of these, 2205 (93%) were included in the study. The 6.8% excluded (i.e., 160 families) had either moved away from the area before they could be visited or refused to cooperate in the study (table 1). The analysis that follows has been based upon the infants born to these families. After exclusions—for example, multiple births—2149 infants were eligible for study. Over the five years of follow-up losses inevitably occurred from the original population; these were small and are unlikely to have seriously biased the findings in the later years of follow-up.

Health visitors, who received special training, administered a questionnaire to the parents, when, as part of their

TABLE 1—SURVEY POPULATION OVER THE FIVE YEARS OF FOLLOW-UP

No. of families with newborn infants born July 1, 1963, to June 30, 1965		No. of index infants at annual follow-up					
Total	Cooperated in survey	Initial visit	First	Second	Third	Fourth	Fifth
2365	2205	2149	2122	2109	2096	2097	2095

routine duties, they visited the infant and mother at home within fourteen days of the delivery. At this visit a number of items were recorded, including birth-weight in pounds to the nearest pound below.

The health visitor also administered a questionnaire which included questions on respiratory symptoms and smoking habits. In this paper positive responses to the question "Do you usually bring up any phlegm from your chest first thing in the morning in the winter?" has been used as evidence for parental respiratory disability. To elicit smoking habits the questions were: "Do you smoke?" If answered "yes", the parent was classified as a present smoker. If answered "no" the parent was asked "Have you ever smoked?" If the answer was "yes", then the parent was classified as an ex-smoker. If answered "no" the parent was asked "Have you ever smoked as much as one cigarette a day for as long as a year?" An answer "no" classified parents as non-smokers. The present smokers were also asked "How many cigarettes are you smoking now?" The validity of the answers to these questions has already been established.<sup>1</sup>

The families were followed up annually for the next five years by postal questionnaires. Each year parents were asked the following questions. For the infant, "Has he/she had in the past twelve months bronchitis? Pneumonia?" For the parents, "Did you usually bring up any phlegm from your chest first thing in the morning last winter?" Smoking habits were assessed using the question "Do you smoke?" If "yes", "How many are

you smoking now?" The validity of answers to the question on infant bronchitis and pneumonia was assessed by checking, in a sample, the parents' account of such an illness with the family doctor's case-notes. The level of agreement was adequate and corresponded to that obtained in other studies where mothers were asked about their children's past health. The validity of the question on phlegm production in the parents has also been established.<sup>2</sup>

In the tables that follow, parents have been classified according to their smoking habits. Parents who at the initial visit had never smoked, and at the first and subsequent follow-ups had not taken up the habit, were classified at each follow-up as non-smokers. In the same way parents who at the initial visit were present smokers, and at the first and subsequent follow-ups did not give up the habit, were classified on each occasion as present smokers. There remained a further group of parents who had changed their habits. These included parents who at the initial visit were ex-smokers. They had been permanently allocated, irrespective of whether or not they took up smoking again, to the "ex-smokers or changed habits" group. In addition there is a further group of parents who were either non-smokers or smokers at the initial visit but who changed their habits during their follow-up. When this occurred they were reclassified permanently as members of the "ex-smokers or changed habits" group. In this way, for example, parents who were smokers at the initial and first and second follow-up visits would be classified as such at these follow-ups. If on the third follow-up they gave up smoking they would be moved to the "ex-smoker or changed habits" group for that and subsequent follow-up years. This method of classification ensures that at each follow-up year the group of "non-smoking" and "present smoking" parents contains parents with consistent smoking habits. The diminishing numbers at each follow-up in these two groups is a result of parents changing their habits and is balanced by the increasing numbers in the "ex-smokers and changed habits" group. The totals in these tables do not correspond to those in table 1. This is accounted for by the exclusion of single-parent families and by absent data.

### Results

The annual incidence per 100 children of pneumonia and bronchitis is given in table II by parents' smoking habit. Parents have been classified into one of four groups: (1) both parents non-smokers; (2) one parent smoker, the other non-smoker; (3) both parents smokers; (4) both parents ex-smokers, or one an ex-smoker, or parents who changed their smoking habits during the study. The incidence of pneumonia and

TABLE II—PNEUMONIA AND BRONCHITIS BY PARENTS' SMOKING HABITS

Year of follow-up	Annual incidence per 100 children (absolute numbers in parentheses) of pneumonia and bronchitis				All
	Both non-smokers	One smoker	Both smokers	Both ex-smokers or one ex-smoker, or smoking habit changed	
1	7.8 (372)	11.4 (552)	17.6 (478)	9.2 (675)	11.5 (2077)
2	8.1 (358)	9.3 (494)	8.9 (438)	7.4 (758)	8.3 (2045)
3	7.0 (342)	10.2 (460)	9.1 (396)	8.9 (834)	8.9 (2032)
4	6.4 (323)	8.3 (408)	9.0 (357)	8.4 (382)	8.5 (1970)
5	7.5 (319)	6.7 (374)	6.5 (340)	6.6 (954)	6.7 (1669)

bronchitis in the infant shows a gradient by parents' smoking habit in the first year of life. Incidence is lowest in infants with both parents non-smokers, highest where both parents smoke, and lies between these values where one parent smokes. This is a statistically significant gradient ( $p < 0.0005$ ). In subsequent years there is no such clear gradient.

In table III parents have been classified both by their smoking habits and by their response to the question "Did you usually bring up any phlegm from your chest first thing in the morning in the last winter?" In all categories except one, the incidence within a smoking category is higher among children where one or both parents have winter morning phlegm than in children whose parents are both free of this symptom. Some of the incidence-rates in the children—in particular those whose parents are both non-smokers and who have winter morning phlegm—are based upon small numbers and therefore may not be wholly reliable. On the other hand, the incidence-rates in children where neither parent has symptoms, whether they smoke or not, are based upon substantial numbers. In them in the first year of life a consistent gradient is seen in the incidence of pneumonia and bronchitis in the children in relation to the parents' smoking habits. The rates are lowest in children of non-smoking parents and highest where

TABLE III—PNEUMONIA AND BRONCHITIS IN THE FIRST FIVE YEARS OF LIFE BY PARENTS' SMOKING HABIT AND MORNING PHEGM

Year of follow-up	Annual incidence per 100 children (absolute numbers in parentheses) of pneumonia and bronchitis									
	Both non-smokers		One smoker		Both smokers		Both ex-smokers or one ex-smoker or smoking habit changed		All	
	N	0/2	N	0/2	N	0/2	N	0/2	N	0/2
1	7.6 (345)	10.3 (29)	10.4 (424)	14.8 (128)	15.3 (399)	23.0 (199)	8.2 (546)	13.2 (129)	10.1 (1452)	16.7 (425)
2	8.1 (322)	8.3 (36)	7.1 (365)	15.3 (129)	8.7 (286)	9.2 (152)	6.5 (599)	10.7 (159)	7.4 (1572)	11.3 (476)
3	6.9 (305)	8.1 (37)	10.5 (353)	9.4 (107)	7.9 (242)	11.0 (154)	8.2 (661)	11.6 (173)	8.4 (1561)	10.6 (471)
4	8.0 (287)	11.1 (36)	7.5 (306)	10.8 (101)	7.6 (236)	11.6 (121)	8.2 (695)	9.1 (187)	7.9 (1524)	10.3 (446)
5	6.7 (285)	14.7 (34)	5.4 (267)	9.4 (107)	5.0 (208)	10.6 (132)	6.4 (737)	7.3 (219)	5.9 (1497)	9.1 (492)

N = neither with winter morning phlegm. 0/2 = one or both with winter morning phlegm.

TABLE IV—PNEUMONIA AND BRONCHITIS BY NUMBER OF CIGARETTES SMOKED PER DAY BY PARENTS AND WINTER MORNING PHEGM

Year of follow-up	Annual incidence per 100 children (absolute numbers in parentheses) of pneumonia and bronchitis									
	Both non-smokers		One or both smokers* of following number of cigarettes per day†:							
			1-14		15-24		25 and over			
	N	O/S	N	O/S	N	O/S	N	O/S	N	O/S
1	7.4 (343)	10.3 (29)	10.4 (269)	15.1 (53)	11.1 (171)	14.5 (76)	15.2 (323)	23.2 (138)		
2	8.1 (322)	8.3 (36)	5.2 (231)	16.4 (55)	8.6 (151)	14.5 (62)	9.7 (269)	9.8 (164)		
3	6.9 (305)	8.1 (37)	11.2 (206)	8.6 (58)	8.2 (146)	9.5 (42)	8.6 (243)	11.2 (161)		
4	8.0 (287)	11.1 (36)	5.5 (163)	13.3 (45)	7.4 (136)	11.5 (52)	9.1 (243)	10.3 (126)		
5	6.7 (285)	14.7 (34)	6.3 (144)	11.4 (44)	4.4 (113)	7.6 (53)	4.1 (216)	10.6 (142)		

\* Excluding parent pairs where one or both are ex-smokers or changed smoking habit.

† Includes tobacco and cigars expressed as cigarette equivalents (see Todd 17).

N=neither with winter morning phlegm. O/S=one or both with winter morning phlegm.

both parents smoke. In children over the age of a year there is, however, no consistent gradient.

Exposure of the child to cigarette smoke may be more precisely estimated from the total daily cigarette consumption of both parents. In table iv the incidence of pneumonia and bronchitis is given for parent pairs smoking between them 1-14, 15-24, and 25 or more cigarettes per day, by the presence of winter morning phlegm. A clear gradient of increasing incidence is seen in the first year of life that is independent of the presence of winter morning phlegm and is of the same size as that in table iii. In the second year and thereafter the pattern is not consistent and thus does not suggest an effect of exposure to tobacco smoke at ages over one year.

The gradients of incidence, particularly those attributable to passive smoking in the first year of life, could result from other factors which are known to influence respiratory disease in infancy—for example, social class and family size. These factors might account for the gradients if children of low social class or of large family size were concentrated in families where the parents smoked or had chest symptoms. That these factors did not explain the observed gradient can be seen in tables v and vi. In table v, the findings for social class III alone are

examined. The patterns for pneumonia and bronchitis for all children in the first year of life persist. Similarly, in table vi, where the data are subdivided by the number of siblings in the family, the patterns for pneumonia and bronchitis persist within families of the same size. This makes it unlikely that either social class or family size can be responsible for these patterns of respiratory-disease incidence.

The infants of mothers who smoke in pregnancy are, on average, lighter than those of mothers who do not smoke. As infants of low birth-weight are more likely to suffer respiratory illness than normal-weight infants, it is possible that the gradients in respiratory disease observed in the first year of life, and in particular the effects of passive smoking, may be due, indirectly, to maternal smoking during pregnancy. In this study, birth-weight, as expected, shows a

TABLE V—PNEUMONIA AND BRONCHITIS IN THE FIRST YEAR BY PARENTS' SMOKING HABIT AND WINTER MORNING PHEGM FOR SOCIAL CLASS III

Annual incidence per 100 children (absolute numbers in parentheses) of pneumonia and bronchitis									
Both non-smokers		One smoker		Both smokers		Both ex-smokers or one ex-smoker		All	
N	O/S	N	O/S	N	O/S	N	O/S	N	O/S
5.9 (171)	20.0 (15)	9.5 (263)	16.5 (79)	17.1 (217)	23.9 (88)	7.1 (294)	12.1 (66)	9.8 (945)	18.2 (248)

N=neither with winter morning phlegm. O/S=one or both with winter morning phlegm.

gradient by parents' initial smoking habit, and to a lesser extent by winter morning phlegm. Thus parents who smoke have lighter infants than parents who do not smoke. The gradients in the incidence of pneumonia and bronchitis with parental smoking, and with winter morning phlegm, might therefore be partly attributable to differences in birth-weight. However, within different birth-weight categories the gradients for pneumonia and bronchitis with parents' smoking habits persist. Thus differences in birth-weight cannot account for the higher risk of pneumonia and bronchitis in the first year of life in children exposed to the cigarette smoke generated when their parents smoke at home.

### Discussion

An association between the respiratory symptoms

TABLE VI—PNEUMONIA AND BRONCHITIS IN THE FIRST YEAR BY NUMBER OF SIBLINGS AND BY PARENTS' SMOKING HABIT AND WINTER MORNING PHEGM

No. of siblings	Annual incidence per 100 children (absolute numbers in parentheses) of pneumonia and bronchitis									
	Both non-smokers		One smoker		Both smokers		Both ex-smokers or one ex-smoker or smoking habit changed		All	
	N	O/S	N	O/S	N	O/S	N	O/S	N	O/S
0	3.9 (153)	14.3 (14)	5.1 (177)	6.3 (32)	13.3 (165)	12.7 (55)	5.8 (258)	6.4 (47)	6.9 (753)	9.5 (148)
1	8.1 (124)	0 (7)	12.0 (146)	12.0 (50)	13.6 (103)	34.1 (44)	9.4 (178)	17.5 (40)	10.9 (551)	19.9 (141)
2 and more	15.2 (66)	12.5 (8)	15.8 (101)	23.9 (46)	22.5 (71)	25.0 (40)	11.6 (110)	16.7 (42)	15.8 (348)	23.3 (136)

N=neither with winter morning phlegm. O/S=one or both with winter morning phlegm.

in parents and in their school-age children was reported by Colley.<sup>4</sup> The present study demonstrates that this association is also found in younger children as early as the first year of life. The nature of this association, as Colley noted, is not clear. He concluded that it was unlikely to be an artefact due, for example, to parents with symptoms over-reporting symptoms in their children. In the present study a sample of parents had their account of respiratory illnesses in their children checked against the doctors' records. The close agreement between these two accounts makes it unlikely that over-reporting in families where parents have symptoms has occurred to any important extent.

The association could be a result of shared genetic susceptibility to respiratory disease between parents and children, to living in the same home environment, and to cross-infection within the family. Twin studies in adults have not been notably successful in assessing the genetic contribution to adult chronic respiratory disease, and no studies have yet been reported where this aspect was investigated in parents and their children. The contribution made by the other factors to this association can, at present, only be guessed at.

Passive smoking by the infant, after differences in birth-weight and parental respiratory symptoms have been allowed for, increases the risk to the infant of pneumonia and bronchitis in the first year of life. When both parents smoke, this risk is almost double that of infants with non-smoking parents. The findings confirm and extend those of Harlap and Davies.<sup>3</sup> These workers did not, however, have information on fathers' smoking habits, nor did they take account of parents' respiratory symptoms.

A picture has thus emerged of a serious risk to infants in the first year of life from exposure to their parents' cigarette smoke. In contrast, between one and five years of age, there does not appear to be any important effect of passive smoking in increasing the risk of pneumonia and bronchitis. Colley,<sup>4</sup> in 6-14-year-olds also found no association between passive smoking and the prevalence of chronic cough.

The estimates of children's exposure to cigarette smoke in this study are crude, being based either on whether parents were smokers or not, or on their total daily cigarette consumption. The smoke exposure of the children may have been overestimated, since parents—in particular the father—will smoke outside the home, or at times when the infant is not present. The effects on the child may thus have resulted from exposure to levels of cigarette smoke less than those suggested by our study.

The evidence from this study, taken with that of Harlap and Davies,<sup>3</sup> provides convincing reasons for warning parents who smoke of the risks this entails for their children both from the direct effect of their cigarette smoke and from the presence of their respiratory symptoms. Attacks of pneumonia and bronchitis, particularly in the first year of life, can still result in infant death despite prompt and vigorous treatment. In those that survive such illnesses and recover clinically, the evidence points to some damage to the respiratory tract as indicated by an increased prevalence of chest symptoms and deficits in ventilatory function found in later childhood.<sup>2,4</sup> The

longer-term consequences of such childhood illnesses have been underlined by the findings in a cohort of infants followed to the age of 20.<sup>5</sup> At this age the prevalence of chronic cough, after allowing for current smoking habits, social class of father, and air-pollution exposure, was higher in those with a documented history of a chest illness under the age of 2 years than in those without this history. If, by the age of 20, such long-term effects are found, these could persist into middle and late adult life and contribute to the evolution of chronic respiratory disease.

Opportunities for the prevention of serious respiratory disease in infancy and childhood are few. If parents who smoke give up the habit they can reasonably expect to lose, or at least experience an improvement in, their respiratory symptoms. This might well result in reduction of respiratory illnesses in their children. At the same time the absence of cigarette smoke in the home could be expected to diminish the risk of attacks of pneumonia and bronchitis in their children during the first year of life.

This study was conducted jointly with the Health, Welfare, and Children's Department of the London Borough of Harrow, and we would particularly like to thank the Superintendent Health Visitors and their staff, the Senior Administrative Assistant in the Personnel Health Section and his staff, and others who took part for their help and cooperation in this study. Our thanks go to the fieldworkers from the Department of Community Medicine for the maintenance of the records and for their diligence in carrying out the fieldwork during the five years of follow-up. We are also grateful to the statistical assistants of the department for carrying out the analysis of the data.

This study has been supported, in part, by a grant from the Department of Health and Social Security for which we are very grateful.

#### REFERENCES

- Holland, W. W., Kessop, H. S., Colley, J. R. T., Cormack, W. *Br. J. prev. soc. Med.* 1969, 2, 77.
- Krueger, D. R., Rogot, E., Blackwelder, W. C., Reid, D. D. *J. chron. Dis.* 1970, 23, 411.
- Butler, N. R., Alberman, E. D. (editors). *Perinatal Problems*. Edinburgh, 1969.
- Colley, J. R. T. *Br. med. J.* 1974, ii, 201.
- Harlap, S., Davies, A. M. *Lancet*, 1974, i, 929.
- Holland, W. W., Hall, T., Bennett, A. E., Elliott, A. *Br. med. J.* 1969, ii, 205.
- Colley, J. R. T., Reid, D. D. *ibid.* 1970, ii, 213.
- Bland, J. M., Holland, W. W., Elliott, A. *Respir. Physiol.* (in the press).
- Colley, J. R. T., Douglas, J. W. B., Reid, D. D. *Br. med. J.* 1973, iii, 195.
- Todd, G. F. *Statistics of Smoking in the U.K.* London, 1972.

"The atomic physicists were as clever, as modest, as self-seeking, as mean, as argumentative and just as concerned for humanity as the microbe hunters. The physicists worked to produce a weapon of war, but there is no real evidence that the nationalistic arguments which convinced them that their efforts were right and just were any different from those that so affected Koch and Pasteur half a century earlier; and the intellectual challenge was just as great, and grappling with it just as enjoyable. . . . The physicists' work was widely seen as being culpable because it was applied to the taking of life; the first two atomic bombs did so on a vast and horrifying scale. But it was Pasteur, and not some atomic physicist, who in 1870 said of the Germans, 'I want to see the war prolonged into the depths of winter, so that all those vandals confronting us shall perish of cold and hunger and disease.'"—ROBERT REID, *Microbes and Men*; p. 168. London: B.B.C. Publications. 1974. £2.50.

2023379613



Holma, B., Winding, O. "Housing, Hygiene, and Health: A Study in Old Residential Areas in Copenhagen" Archives of Environmental Health (March/April): 86-93, 1977.

ABSTRACT. The effect of 109 social, medical, housing, and hygienic factors on morbidity of 2,096 individuals was studied in 881 apartments in Copenhagen. "Thriving" (satisfaction), followed by "housing standard" and "personal hygiene," turned out to be the most prominent predictor for health. "Thriving of parents" was also important for the health of children. Excluding "thriving" in the analyses, "housing standard" and "personal hygiene" or components of these group factors were the important predictors for the health of the population studied, except for children below 3 years of age. For the health of these, the number of rooms used for sleeping purposes was the best predictor. The only other parameter found to influence the morbidities investigated was the total yearly income of the family, which was found to be a secondary predictor for adult morbidity during the last month of the investigation (March 1973). The analyses applied were Pearson correlation, AID-program, factor and multiple regression analyses.

2023379615

30. Villanueva, E.C.; Jennings, R.W.; Burse, V.W.; and Kumbrough, R.D. 1975. Evidence of chlorodibenzo-p-dioxin and chlorodibenzofuran in hexachlorobenzene. *J Agric Food Chem* 22:916-17.

31. Vos, J.G.; Koeman, J.H.; Van der Maas, H.L.; ten Noever de Brau, M.C.; and de Vos, R.H. 1970. Identification and toxicological evaluation of chlorinated dibenzofuran and chlorinated naphthalene in two commercial polychlorinated biphenyls. *Food Cosmet Toxicol* 8:625-32.

# Housing, Hygiene, and Health

## A Study in Old Residential Areas in Copenhagen

BO HOLM, M.D.  
OLE WINDING, M.Pharm.  
Institute of Hygiene  
University of Copenhagen

### ABSTRACT

The effect of 109 social, medical, housing, and hygienic factors on morbidity of 2,096 individuals was studied in 881 apartments in Copenhagen. "Thriving" (satisfaction), followed by "housing standard" and "personal hygiene," turned out to be the most prominent predictor for health. "Thriving of parents" was also important for the health of children. Excluding "thriving" in the analyses, "housing standard" and "personal hygiene" or components of these group factors were the important predictors for the health of the population studied, except for children below 3 years of age. For the health of these, the number of rooms used for sleeping purposes was the best predictor. The only other parameter found to influence the morbidities investigated was the total yearly income of the family, which was found to be a secondary predictor for adult morbidity during the last month of the investigation (March 1973). The analyses applied were Pearson correlation, AID-program, factor and multiple regression analyses.

STUDIES HAVE revealed that factors such as overcrowding, lack of basic sanitation (e.g., cold or hot water supply), garbage accumulation, and poor construction with leaky roofs or cracked walls exert substantial influence on health. However, extreme conditions are seldom found in developed countries, and the relative importance of various factors in housing conditions is difficult to analyze. Thus, contradictory or negative results have been obtained in the developed countries with respect to the relative importance of overcrowding, socioeconomic conditions, occupation, education, housing conditions, rehousing, etc., as they may affect morbidity.<sup>1</sup>

During childhood, the area of residence, parents' social level, family size, history of respiratory diseases, and impairment of ventilatory function of the lungs influence health in adult life.<sup>2-4</sup> A survey covering the field of housing and health was made by A.E. Martin<sup>5</sup> in the United Kingdom, and by V. Christensen<sup>6</sup> in Scandinavia.

### Method

Six residential areas of Copenhagen were studied. Within each area we sampled a cluster of successive house numbers and stories. We included an equal number of men and women. The districts under study represented older houses in the central part of Copenhagen.

District One (Oesterbro) is characterized by wide streets with trees and small parks. Buildings are mainly large, fashionable-looking, older apartment houses containing large well-lighted flats with up to ten rooms or more, some with a desirable view. In this area, 183 families were questioned (89 males and 94 females).

District Two similarly consists of large, well-kept apartment houses with an exclusive location by one of the artificial lakes of Copenhagen (Sortedsøen). The flats are large and sunny, but about 100 m from the lake the

area borders on one of the most closely built-up and densely populated areas in Copenhagen (District Five), resulting in an inevitable interaction between the extremes of the social classes, especially as far as children are concerned. In this area, 91 families were questioned (33 males and 58 females).

District Three, nicknamed "Potatorows," is on the opposite side of the same lake. The buildings are low, well-separated, single-family houses about 100 years of age. Each house contains up to three small flats. The original quality of the houses was poor (small and damp, without shower, bath tub, or hot water installations). In front of the houses are small, well-kept gardens, and the friendly surroundings have attracted new social groups to the area. Simultaneously, extensive interior modernization has taken place, especially concerning hygienic facilities. In this area, 199 families were questioned (71 males and 128 females).

District Four is situated in a closed area between a main road (Oesterbrogade) and a big park. The houses were built in the midnineteenth century, after a cholera epidemic, as dwellings for workers. They are four long, two-story buildings divided into two-storied flats with separate house numbers. The flats are very small, usually not more than 25 m<sup>2</sup>, and without hygienic or sanitary installations. The area includes an assembly building and common houses for bathing and washing. For each group of ten flats there is a chemical lavatory in a small addition to the houses. In front of each flat is a small garden, 10-20 m<sup>2</sup>. In spite of the smallness of the flats and their very limited facilities, the inhabitants find so many compensating qualities in the surroundings that they express general contentment. In this area, 43 families were questioned (22 males and 21 females).

District Five (Ryesgade) is situated alongside District Two, less than 100 m away. It is one of the most popu-

2023379616

lous streets in Copenhagen, and had a population of 70,000 people before partial demolition began in the area. The buildings are five- and six-story apartment houses with up to three back buildings. An ordinary complex will consist of a front building and two back buildings. The flats are small and insufficiently furnished with hygienic facilities. Heating is mainly separate for each room and is dependent on oil stoves or the like. Daylight in the flats is scanty, and recreation facilities for children and grown-ups are nonexistent in the district. In this area, 214 families have been questioned (101 males and 113 females).

District Six is situated in the inner city (Noerrebro) and has the nickname "the black square." The buildings in the area must be described as slums and are partly condemned. Quality of flats is comparable with that in District Five, but the area is generally considered the worst of the districts studied. Typical flats in districts Five and Six have two rooms and awkward entrance facilities. Narcotics are said to be a problem in this district. In this area, 135 families were questioned (63 males and 72 females).

The respondent was asked to fill out a questionnaire of 109 questions with alternate and/or grouped answers. Instruction was given by the interviewers (medical students), who returned 1½ hours later to collect the forms after having given supplementary instructions, as necessary. Up to five repeated attempts were made to contact persons who were not available or did not answer. The interviewers received their instructions partly as a group at an evening course and partly individually before visiting the districts.

Univariate tables were made for all variables. From a Pearson correlation matrix a screening selected all significant correlations. Corresponding bivariate tables were made in order to study the correlations more closely.

Morbidity, the dependent variable, was defined as the number of episodes of illness, regardless of the duration. All other answers were considered independent variables. We used an Automatic Interaction Detector (AID) program to split the material into groups of respondents characterized by discrete values of one or more (uncorrelated) predictors. The principle for the split is a successive search for the predictor that gives the maximum difference between sums of squares for the dependent variable in the two groups. In this paper, the AID results are illustrated as figures forming "three-structures" of "original" and "split" groups.

## Results

### Frequency Tables

From 930 initial questionnaires the number of cases obtained was 881, covering 2,096 individuals—a response rate of 94.7%. The sample amounted to 12% of the total population in the areas examined; i.e., in District One, 10.5%; in District Two, 19.0%; in District Three, 10.5%; in District Four, 5.5%; in District Five, 12.0%; and in District Six, 17.0% of the population based on the statistical yearbook for Copenhagen 1973.<sup>7</sup>

A two-way display of age and sex in the population investigated is shown in Figure 1. Other characteristics of the different areas are given in Tables 1 and 2. From Table 1 it can be seen that the smallest dwellings (< 25 m<sup>2</sup>) are most frequent (64.8%) in District Four and the largest ones (> 200 m<sup>2</sup>) are to be found in District One and Two.

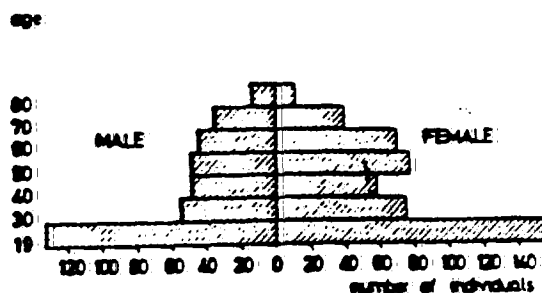


Fig. 1. Respondents' distribution by age and sex.

A low standard of housing is found in Districts Four, Five, and Six, characterized by, among other things, drafts and cold and a lack of hot water or bath tub, especially in District Four, where bathing facilities do not exist. Also in District Four, water closets outside the dwellings are found in up to 90.5% of the cases. However, in this district most people are content with their area of residence and present excellent personal hygiene as compared with the other districts (Table 1).

The highest average figure for overcrowding, measured as individuals per room (kitchen included), was 0.68 in District Five (Table 2). The best housing standards are found in Districts One and Two, while Four, Five, and Six are inferior in this respect.

A summarized description of morbidity in the different areas is found in Table 3. On the whole, morbidity was low in District Two and high in District Five for all age groups, the 3- to 6-year-old children being an exception, with higher morbidity in District Three.

The highest morbidities were reported from District Five, which has the lowest housing standard next to that of District Four. In this latter district the morbidity of the adults was high, but the effect of environment and other factors on child morbidity could not be evaluated on account of the unusually small number of children living in this district.

The lowest morbidity was found in District Two. This district was rather homogeneous and did not show the large variation in housing standards found in other districts.

In District Five and especially in District Six the "thriving" was lowest. Almost every second person expressed an absolute intention of changing to another dwelling and district. However, in the other districts that represented old houses of low standards, nobody expressed any great wish or intention to move. Those who wished to move from District Four, for instance, represented only 7% and 4.8% of the population, with complaints about dwelling and area of residence, respectively. The people in this district have given public expression to their desire to preserve the area in its present condition, contrary to the authorities' intention to clear the area because of the low hygienic standard of the buildings.

### Correlation Matrix

From the correlation matrix some associations between morbidity and other examined variables may be suggested. For 1- to 6-year-old children in these areas of Copen-

2023379617



Table 1.--Some Characteristics of the Six Residential Districts in Copenhagen

CHARACTERISTICS	"ONE" N %	"TWO" N %	"THREE" N %	"FOUR" N %	"FIVE" N %	"SIX" N %
Dwelling < 25 sq.m.	0 0.0	4 4.5	17 9.2	27 64.3	18 8.5	19 14.4
Dwelling > 100 sq.m.	76 43.7	44 49.4	28 15.2	1 2.4	24 11.4	15 11.4
Dwelling > 200 sq.m.	23 13.2	5 5.6	2 1.1	0 0.0	0 0.0	0 0.0
Dwelling > 6 rooms	28 15.2	14 15.2	17 8.5	0 0.0	8 3.6	9 6.6
Draft and cold	8 4.3	7 7.7	14 7.0	4 9.1	46 21.1	32 23.5
Hot water lacking	8 4.3	6 6.7	31 16.2	29 78.4	114 54.8	61 46.9
Shower lacking	22 11.9	17 19.5	90 47.1	36 100.0	175 83.3	108 35.7
Bath tub lacking	38 20.5	22 26.5	129 69.4	36 100.0	196 95.1	118 95.9
Single room heating	25 14.0	6 6.7	46 24.7	26 65.0	106 53.0	50 39.4
Closet outside dwell.	4 2.2	6 6.7	17 8.6	38 90.5	35 16.1	24 18.0
Danger of accidents in dwelling	14 7.7	7 7.7	31 15.7	9 21.4	63 29.0	43 32.1
Contentment with dwelling	65 35.1	48 52.2	83 41.3	14 31.8	27 12.3	17 12.5
Contentment with "district"	77 41.6	43 46.7	105 52.2	36 83.7	27 12.3	14 10.3
Occup.: Workers	17 9.5	2 2.2	18 9.2	8 19.0	69 32.2	46 34.3
Absolutely intent on changing dwelling	34 18.5	12 13.2	36 18.2	3 7.1	106 47.9	74 55.2
Income > 100,000 d.kr. per year	40 23.1	16 18.2	16 8.4	0 0.0	6 3.0	2 1.5
Education level high	44 24.4	24 26.7	73 36.5	15 35.7	19 9.7	22 16.3
Education level low	57 31.7	32 35.6	75 37.6	18 42.9	153 72.1	96 71.1
Never using shower	32 18.2	13 15.7	39 19.8	3 7.0	48 22.9	17 13.3
Never using bath tub	45 24.7	28 33.7	108 55.4	23 56.1	139 68.5	86 68.8
> 10 cigarettes per day	33 27.3	19 38.8	32 28.3	16 48.5	55 37.7	39 40.2

N = Number of respondents  
 % = Percentage of respondents within the district

2023379618

hagen, reported morbidity in the period March 1972-March 1973 was correlated with the parents' dissatisfaction with their partner's occupation ( $P < .01$ ), the number of small children in the family ( $P < .01$ ), the parents' dissatisfaction with the environment and spare-time facilities within

the area of residence ( $P < .05$ ) and with their housing standard ( $P < .05$ ), as well as with parents' morbidity ( $P < .05$ ), and common colds in particular ( $P < .01$ ). For the 7-18 year age group, morbidity was correlated with the morbidity of the parents ( $P < .01$ ), especially in regard to the parents'

Table 2.-Population Characteristics of the Six Residential Districts in Copenhagen

Characteristics	ONE		TWO		THREE		FOUR		FIVE		SIX	
	N	%	N	%	N	%	N	%	N	%	N	%
Men responding	89	48.6	33	36.3	71	35.7	22	51.2	101	47.2	63	46.7
Women responding	94	51.4	58	63.7	128	64.3	21	48.8	113	52.8	72	53.3
Children 7-18	58		47		42		0		76		41	
Children 3-6	27		12		26		1		26		25	
Children 1 & 2	25		16		18		3		31		23	
Other family members	172		115		149		15		177		111	
Individuals	460		281		434		62		524		335	
Individuals per room kitchen incl.		0.48		0.52		0.52		0.58		0.68		0.66

N= Number of respondents

%= Percentage of respondents within the district

Table 3.-Self-Reported Morbidity of More Than One Day During the Last 12 Months in Different Age Groups within the Districts

Characteristics	ONE		TWO		THREE		FOUR		FIVE		SIX	
	N	%	N	%	N	%	N	%	N	%	N	%
Adult	94	53.4	43	47.3	109	56.5	26	65.0	151	69.9	84	63.6
Children 7-18	58	63.0	47	43.3	42	62.5	0	0	76	76.4	41	64.3
Children 3-6	22	60.0	12	44.4	26	76.0	2	50.0	26	64.5	25	56.5
Children 1 & 2	25	68.0	16	65.0	18	77.3	3	60.0	31	78.4	23	75.9

N= Number of respondents

%= Percentage of respondents within the age group in the district

2023379619

respiratory diseases ( $P < .05$ ).

Morbidity of adults was correlated with dissatisfaction with their partner's occupation ( $P < .01$ ), the quality of housing ( $P < .01$ ), and with dissatisfaction with the environment in the district, i.e., the standard of the district in relation to the other districts ( $P < .05$ ). Respiratory symptoms in particular seemed to be responsible for their morbidity, expressed as coughing, phlegm production, and wheezing in the chest. Illnesses of the adults during the last month of study (March 1973) were also related to these respiratory symptoms ( $P < .05$ ) and coincided with an increased morbidity among the children ( $P < .05$ ).

In addition to the cited results, a great number of correlations that did not concern morbidity were found. None of these was surprising.

### AID Analysis of Single Predictors

Analysis of morbidity of adults within the last 12 months showed a split into seven groups (Fig. 2). Fatiguing work at home formed the basis for the primary split. The group with outspoken complaint of fatiguing work and with higher morbidity showed a secondary split into a still higher morbidity level in the socially worse districts, namely, Districts Five and Six, and a lower morbidity for those living in Districts One, Two, Three, and Four. For the other group with little or no fatiguing work at home, the secondary split was based on the predictor "contentment with the dwelling." Those not content with their dwelling were further split by the predictor "drafts and cold," and those satisfied with their dwelling were split once more by "fatiguing work at home." Contentment with one's occupation caused a further split within this last group.

The corresponding morbidity of adults within the last month (March 1973) showed a primary split based on the

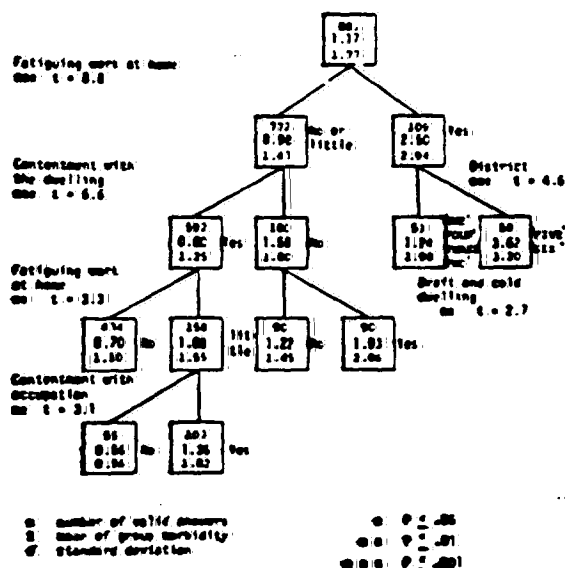


Fig. 2. Morbidity of adults during 12 months: AID analysis of single predictors.

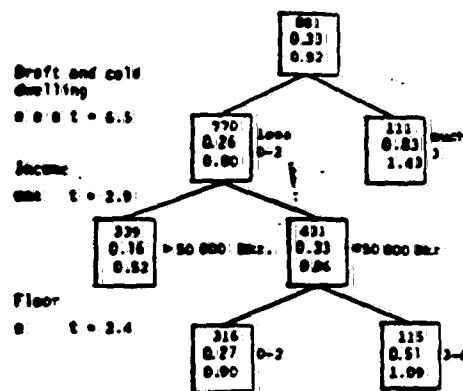


Fig. 3. Morbidity of adults during last month: AID analysis of single predictors. For key to Figures and symbols, see Figure 2.

housing standard, expressed as drafts and cold in the dwelling, while the yearly income of the family became a secondary predictor for those complaining less about drafts and cold in the dwellings (Fig. 3). For those with a higher income, the level of the apartment above the street was a third predictor for their morbidity.

In a separate analysis of the 228 single individuals included in the study, it was found that the morbidity during the last year was predicted by fatiguing work at home. For those not stressed by this factor, morbidity was predicted by districts (Fig. 4). The morbidity of the 653 married persons was primarily predicted by their contentment with their dwellings. Complainers who had a higher morbidity were further split by the presence or absence of dampness in the dwelling, and of these, those without

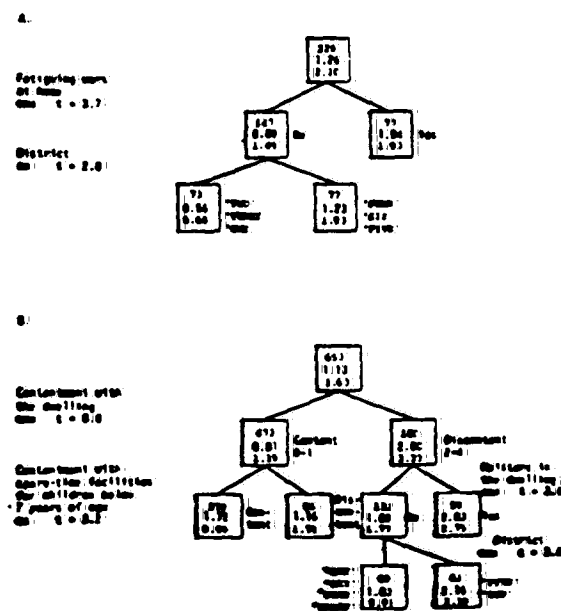


Fig. 4. Morbidity of single persons (A) and married persons (B). AID analysis of single predictors. For key to Figures and symbols, see Figure 2.

2023379620

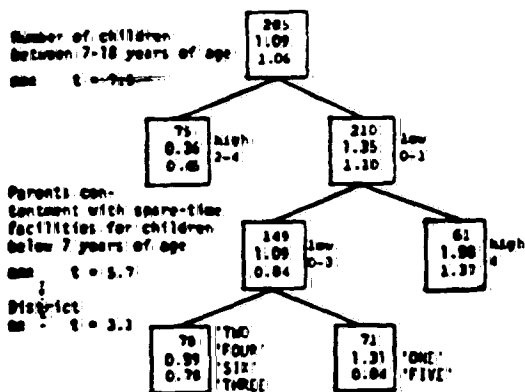


Fig. 5. Morbidity of children of 1-18 years of age: AID analysis of single-predictors. For key to Figures and symbols, see Figure 2.

dampness had a lower morbidity and showed a tertiary split by district. Morbidity for the group with high contentment with their dwelling in the primary split was in the next step predicted by their contentment with spare-time facilities for children under 7 years of age. Those content with the facilities had a lower morbidity (Fig. 4).

The mean morbidity of all children studied was increased in families with few children in the age group 7-18 years of age. The secondary predictor was their parents' contentment with the spare-time facilities for the children under 7 years of age. Children of parents who were least content with these facilities had the highest morbidity.

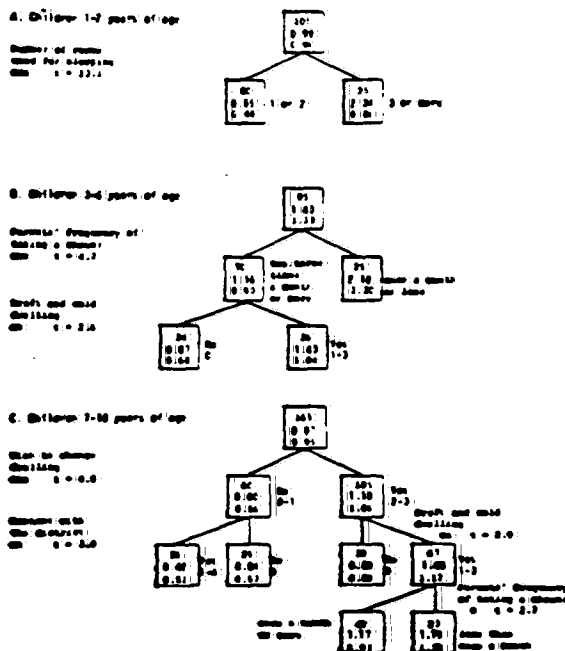


Fig. 6. Morbidity of children 1-2 years of age (A), 3-6 years of age (B), and 7-18 years of age (C). AID analysis of single predictors. For key to Figures and symbols, see Figure 2.

A third predictor for morbidity was the area of residence (Fig. 5).

The morbidity of the youngest children investigated, 1 and 2 years of age, was predicted by the number of rooms used for sleeping purposes at home (Fig. 6). The best predictor for the morbidity of children 3-6 years of age was the personal hygiene of their parents, measured as the frequency of taking showers (Fig. 6). Thus, parents taking a shower with a frequency of less than once a month were associated with an increased morbidity of this age group of children. For families with better hygiene in this respect, the housing standard, expressed as drafts and cold in the dwelling, became another predictor for the morbidity of these children.

The morbidity of children 7-18 years of age (Fig. 6) was in the first place predicted by the parents' strong wish to change their dwelling, and in the second place by the discomfort from drafts and cold. The third predictor was the parents' personal hygiene, i.e., their frequency of taking a shower. The group with low morbidity in the first step was further split by the parents' contentment with the area of residence.

#### AID Analysis of Grouped Predictors

After the split of the material into homogeneous morbidity groups on the basis of single predictors, we combined predictors into group factors: "thriving," "housing standard," "personal hygiene," "tobacco consumption," and "alcohol consumption." The specific procedures may be obtained from the authors.

"Thriving" refers to the level of contentment as studied by the following parameters: respondent and partner's contentment with dwelling, district, neighbors, and occupation; their desire to move or to change place of

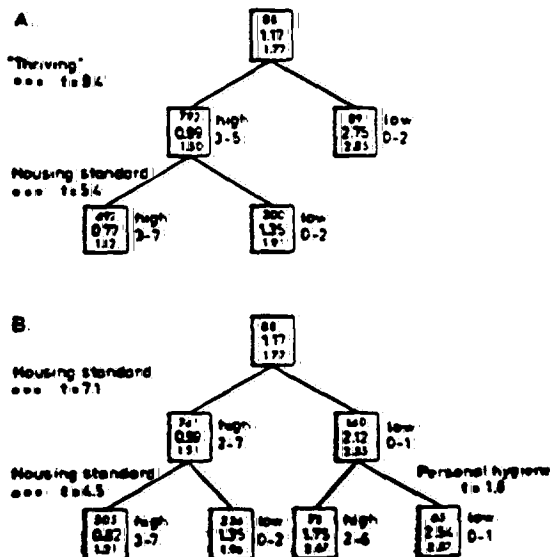


Fig. 7. Morbidity of adults. "Thriving" factor included (A) and excluded (B) in the AID analysis of grouped predictors. For key to Figures and symbols, see Figure 2.

occupation; and the respondent's contentment with spare-time facilities for children 3-6 and 7-18 years old. The "thriving" factor eliminated the other group factors, with the exception of "housing standard," as a predictor for splitting into groups by morbidity during the last year (Fig. 7). As thriving may be questionable as an independent variable, analysis was also undertaken with this factor excluded. Such an analysis yielded "housing standard" as the best predictor for adult morbidity, followed by "personal hygiene" (Fig. 7).

In analyses in which the adults' cases of illness, inclusive of chronic symptoms, were analyzed in an analogous way, "thriving" turned out to be the best predictor, followed by "housing standard" for the high "thriving" and "personal hygiene" for the low "thriving." With better hygiene, "thriving" again became the dominant predictor for those in the low "thriving" group, while "housing standard" was more important for those in the group with high "thriving." In a corresponding analysis where "thriving" was excluded, only "housing standard" remained as a predictor for morbidity.

The morbidity of adults during the last month (March 1973) was best predicted by their "thriving," followed by "housing standard" for those with high "thriving." Exclusion of "thriving" from the analysis yielded "housing standard" as the only predictor for morbidity.

An investigation of the unmarried persons by the AID analysis of grouped factors showed that "personal hygiene" was the only predictor for their morbidity during the last year (March 1972-March 1973); this was true whether the "thriving" factor was included or not. On the other hand, as far as the married respondents were concerned, the AID analysis showed that the "thriving" factor was the dominating predictor for their morbidity during the year of the investigation. For persons with low "thriving" and high morbidity no other predictors turned up. The morbidity of persons with high "thriving" and better health was further predicted by "housing standard," again followed by "thriving." In a corresponding analysis, where the "thriving" factor was excluded, "housing standard" turned out to be the prominent predictor for morbidity of married respondents.

When the respondent units, i.e., the respondents including any other family members, are considered as a target group, and the morbidity of the mean individual in these units is sought, the corresponding AID analysis shows that the predictor "thriving" again occurred as the dominant factor, followed by "housing standard." In a further analysis, when the predictor "thriving" was excluded, "housing standard" once more turned out as the only predictor for morbidity.

#### *Multiple Regression Analysis*

An attempt to use step-wise multiple regression technique (twenty-nine of the fifty-seven most significant variables) to obtain more quantitative evaluations gave as "best" result for the morbidity an explanation of 35% of the total variance, and this was only true for the 7- to 18-year-old children. The corresponding analysis with the variables grouped into factors of "housing standard," "personal hygiene," "alcohol consumption," "tobacco con-

sumption," and "thriving" did not yield more conclusive results.

#### *Discussion*

A comparison between our results and earlier studies in which housing standard and related factors have been investigated, e.g., Vagn Christensen's study in 1956,<sup>6</sup> is difficult, primarily because of the lack of objective measures of the "hygienic standard" used in these studies. Christensen used mortality among children of 0-2 years of age as an indication of low housing standard. Furthermore, our results from 1973 are not comparable with these studies because of the changes which have occurred since then in, for example, the social structure and the standard of living.

On the other hand, many epidemiological studies have not given attention to whether the study's relationships were linear or followed an irregular, logarithmic, or other function. For linear relationships correlation analysis might be sufficient, but for, e.g., irregular relationships such as those for quality of life, the nonlinear dependent AID analysis gives more valuable information. This was one of the reasons we used this form of analysis in our study.

In this study, which is concerned with morbidity in general, the factor "thriving" (satisfaction) was the most prominent predictor for health as compared with other group factors, such as "housing standard," "personal hygiene," "tobacco consumption," and "alcohol consumption." Like morbidity, however, thriving can to a great extent be considered as a function of the society. Thus thriving and morbidity have many connections in common and do not necessarily express a direct connection of causes, even though it is well known that thriving influences our well-being and thereby our health. An interesting aspect of this investigation, however, was that the connection between thriving and morbidity was stronger than the correlation between morbidity and other hygienic and social factors. Furthermore, the most outstanding correlation coefficient found in this study concerned the morbidity of children under 7 years of age and the parents' dissatisfaction with the spare-time facilities for this age group, and, further, the parents' dissatisfaction with their partner's occupation (two of the thirteen components in the group factor "thriving").

That thriving turned out to be the most prominent factor for morbidity in general was surprising, but not many studies have been performed in which the relative importance of this factor is analyzed in comparison with others. However, in 1974 Kato et al.,<sup>8</sup> using four different questionnaires distributed in four cities in Japan, also showed that "subjective feeling of satisfaction" was most significantly correlated with health, and, as they say, "might work to cover shortage of other resources."

The importance of thriving is also reflected in other investigations where, in spite of different definitions, it has been proven to play a prominent role. In Denmark, for instance, E. Pedersen has emphasized in his different works<sup>9</sup> the importance of thriving in the working environment, and has shown that a person's expectations and the fulfillment of these determine the thriving of the person. The studies made by O. Berg in southern Greenland show that there is a connection between morbidity, satisfaction, and hous-

ing conditions, which connection O. Berg related to the special living conditions in this part of arctic Denmark.<sup>10, 11</sup>

In the present study the importance of psychological factors for health is strengthened by the fact that morbidity for adults was predicted by their dissatisfaction with the area of residence, the dwelling, and the partner's occupation. These factors, as well as some habits of the parents (e.g., the frequency of taking a shower) and the physical and psychological contact within the family group (number of sleeping rooms, older siblings, etc.), also influenced the morbidity of the children. In the light of these findings, morbidity appears to be more dependent on psychological factors than on technical and social standards.

The predictor "fatiguing work in the dwelling," which in this study has appeared as a predictor for morbidity, is difficult to estimate; it may reflect many factors and may be in itself partly a causal factor. However, whenever poor housing standard was demonstrated as an important predictor for morbidity, the factor "fatiguing work in the dwelling" may be a causal factor in this relation. This applies especially to Districts Five and Six, where housing standards are poorest, and which more often than not are inhabited by older people.

Overcrowding, i.e., more than 1.5 individuals per room, including the kitchen, could not be demonstrated to have an effect since 0.7 was the highest number found for this factor. The effects of overcrowding by other definitions, such as only one child in families living in one- or two-room apartments,<sup>6</sup> have not been evaluated. The study did not indicate increased morbidity for children with increasing size of the family. Furthermore, in contrast to Christensen,<sup>6</sup> no correlation was found between morbidity and the area of the dwelling. On the contrary, the morbidity of the youngest children increased with the number of rooms used for sleeping.

Almost all other of the 109 different parameters investigated, like civil status, sex, education, and occupation, showed no important statistical associations, with one exception: the total yearly income of the family. This only had influence as a secondary predictor for morbidity, during the last month of the investigation, of adults who had a better housing standard.

The negligible effects of tobacco and alcohol must be evaluated in the light of the fact that morbidity in this study covers morbidity in general. Furthermore, the influence of parents' tobacco smoking on the morbidity of the youngest children of 1-4 years of age, found by D.J. Hammer et al.,<sup>12</sup> could not be confirmed in our study. The relative influence of tobacco and alcohol on specific symptoms and diseases might give other results but was not evaluated in this study.

By and large this study indicated the importance of thriving for the health of people. It should be pointed out that people in some old-fashioned districts fight for the right to stay and to preserve the present environment of the houses, while at the same time up to 50% of people in new flats in the suburbs express a wish to move.<sup>13</sup> This fact seems to indicate that modern planning in Copenhagen

has failed to provide an environment acceptable to people of our time, which was the original intention.

## Conclusion

The results obtained indicate that measures to improve the public health should also aim at increasing the thriving of people in their environment, at home, in their area of residence, and at work, or at least at protecting them from processes that might in any respect disturb their thriving. Community health planning and education should to a greater extent attend to housing standards, spare-time facilities, and efforts to improve personal hygiene.

• • • • •

This work was partly supported by the Danish Medical Research Council and partly by grants from Peter Ryholt's Fond. The authors wish to thank Georg J. Kjoer, M.Sc., for statistical assistance in the selection of suitable methods for screening and analyzing the data.

Submitted for publication May 22, 1975; revised, accepted December 9, 1975.

Article copies are available from: Bo Holma, M.D., Institute of Hygiene, University of Copenhagen, 21, Blegdamsvej, DK-2100 Copenhagen, Denmark.

• • • • •

## REFERENCES

1. 1972. The home environment. In *Health hazards of the human environment*. Geneva: World Health Organization.
2. Holland, W.W.; Halil, T.; Bennett, A.E.; and Elliott, A. 1969. Factors influencing the onset of chronic respiratory disease. *Br J Med* 12: 205-8.
3. Douglas, J.W.B., and Waller, R.E. 1966. Air pollution and respiratory infection in children. *Br J Prev Soc Med* 20: 1-6.
4. Lunn, J.E.; Knowelden, J.; and Handyside, A.J. 1967. Patterns of respiratory illness in Sheffield infant schoolchildren. *Br J Prev Soc Med* 21: 7-16.
5. Martin, A.E. 1967. Environment, housing and health. *Urban Studies* 4: 1-21.
6. Christensen, V. 1956. Boligforhold og Børnesygelighed. M.D. thesis, University of Copenhagen. Copenhagen: Ejnar Munksgaard.
7. *Statistical yearbook 1973*. Copenhagen Statistical Office.
8. Kato, M.; Takatomi, T.; Yamamoto, K.; Kobayashi, S.; and Ishihara, K. 1974. Rapid increase of population density as a possible determinant of mental health. Paper presented at 7th International Scientific Meeting of the International Epidemiological Association, 17-21 August 1974, Brighton, England.
9. Peterson, E. 1968. Trivsel på Arbejdspladsen, I. Copenhagen: Mentalhygiejnisk Forlag.
10. Berg, O. 1974. Bolig- og sygdomsforhold i et sydgrønlandsk distrikt. *Ugeskr Læger* 33: 1863-68.
11. Berg, O. 1973. Den grønlandske bolig i dag. *Tidsskrifter Grønland* (February-March 1973): 11.
12. Hammer, D.J.; Shy, C.M.; Calafore, D.C.; Hayes, C.G.; McClain, K.E.; and Bivens, J.F. 1972. Cigarette smoking, air pollution and socioeconomic status in relation to acute and chronic respiratory disease. Paper presented at American Medical Association Air Pollution Medical Research Conference, October 1972, Chicago.
13. Martini, S. 1974. *Nyere forstædsmiljøer*. Copenhagen: The Danish National Institute of Social Research (publication 61, released through Teknik Forlag).

4

2023379624

Melia, R.J.W., Florey, C.V., Altman, D.G., Swan, A.V. "Association between gas cooking and respiratory disease in children" British Medical Journal 2:149-152, 1977.

SUMMARY: A four-year longitudinal study of the prevalence of respiratory symptoms and disease in schoolchildren and related environmental and socio-economic factors is in progress. We report results for the first year of this study (1973).

A total of 5758 children age 6 to 11 years from 28 randomly selected areas of England and Scotland were examined. In an analysis of the effects on health of possible indoor pollutants, boys and girls from homes in which gas was used for cooking were found to have more cough, "colds going to the chest", and bronchitis than children from homes where electricity was used. The girls also had more wheeze if their families used gas for cooking. This "cooking effect" appeared to be independent of the effects of age, social class, latitude, population density, family size, overcrowding, outdoor levels of smoke and sulphur dioxide and types of fuel used for heating. It was concluded that elevated levels of oxides of nitrogen arising from the combustion of gas might be the cause of the increased respiratory illness.

2023379625



## Association between gas cooking and respiratory disease in children

R J W MELIA, C du V FLOREY, D G ALTMAN, A V SWAN

*British Medical Journal*, 1977, 2, 149-152

### Summary

A four-year longitudinal study of the prevalence of respiratory symptoms and disease in schoolchildren and related environmental and socio-economic factors is in progress. We report results for the first year of this study (1973).

A total of 5758 children aged 6 to 11 years from 28 randomly selected areas of England and Scotland were examined. In an analysis of the effects on health of possible indoor pollutants, boys and girls from homes in which gas was used for cooking were found to have more cough, "colds going to the chest", and bronchitis than children from homes where electricity was used. The girls also had more wheeze if their families used gas for cooking. This "cooking effect" appeared to be independent of the effects of age, social class, latitude, population density, family size, overcrowding, outdoor levels of smoke and sulphur dioxide and types of fuel used for heating. It was concluded that elevated levels of oxides of nitrogen arising from the combustion of gas might be the cause of the increased respiratory illness.

### Introduction

Respiratory disease is a major cause of childhood morbidity. Episodes of respiratory disease have been said to predispose

children to acute respiratory disease in early adulthood,<sup>1</sup> which may in turn predispose them to later chronic respiratory disease—a major cause of morbidity and mortality among older people in the United Kingdom.<sup>2</sup> The burden of chronic respiratory disease might be reduced if environmental hazards known to be associated with acute respiratory disease in childhood were altered or removed.

Outdoor air pollution has been repeatedly shown to be related to the prevalence of respiratory illness in children<sup>3-6</sup> and our data have suggested that the relationship may exist even at relatively low levels of pollution.<sup>7</sup> We examine here the relation between respiratory illness and indoor air pollution arising from cooking fuels. The two fuels predominantly used in the home for cooking are electricity and gas. The former causes negligible pollution, but the latter gives rise to a range of pollutants on combustion.

### Methods

This project was part of a larger study of the health and growth of primary schoolchildren which started in 1972. Twenty-two employment exchange areas in England and six in Scotland were selected from a total of 547 areas by stratified random sampling so that poorer areas were proportionately better represented. Details of the sampling method have been published elsewhere.<sup>8</sup>

The study population consisted of all children aged 6 to 11 in selected primary schools within each of the 28 areas who were followed up in 1973. During this year questions on respiratory illness and the type of fuel used for cooking in the home were added to the questionnaire. Out of 9124 white children seen in 1972 7851 were re-examined in 1973 (86%).

Information about respiratory symptoms experienced during the previous 12 months and episodes of bronchitis and asthma was requested in a self-administered questionnaire completed by the children's parents or guardians.<sup>9</sup> The question about the cooking fuel used at home was: 'Do you cook by electricity, gas, coal, other (if other, please specify)?' There was a similar question for the main fuel used for heating and other questions to elicit socioeconomic information. The children were classified according to their fathers' occupations into the six social class groups defined by the Registrar General.<sup>10</sup> No questions were asked about parental smoking habits.

Outdoor smoke and sulphur dioxide ( $\text{SO}_2$ ) were sampled over 24-hour periods at or near the study schools in 10 of the areas, using the daily smoke  $\text{SO}_2$  sampler.<sup>11</sup>

Department of Community Medicine, St Thomas's Hospital Medical School, London SE1

R J W MELIA, MR, assistant lecturer

C du V FLOREY, MR, senior lecturer

D G ALTMAN, MR, member scientific staff (present address: Clinical Research Centre, Division of Computing and Statistics, Harrow, Middlesex HA1 1UJ)

A V SWAN, MR, senior lecturer

Of the 7851 children 214 were excluded from the analysis because they came from homes in which coal or a mixture of fuels was used for cooking. There was no information on cooking fuels for 84.1 of the remaining 7637 children, which left 6747 children who came from homes in which either electricity or gas only was used for cooking. Data (on age, sex, social class and responses to all six questions on respiratory symptoms and diseases) were complete for 5758 of these children: 3204 lived in houses where electricity was used for cooking and 2554 in homes where gas was used.

## Results and comment

### SIMPLE PREVALENCES

In each case the prevalence of each respiratory symptom and disease was higher in boys and girls from homes where gas was used (table I). The differences in prevalence between the two groups of children were significant ( $P < 0.05$ ) for bronchitis, day or night cough, and colds going to the chest in both sexes and, in girls, for all other symptoms. Prevalence rates were higher in boys than in girls.

### COMPARISONS OF RESPIRATORY ILLNESS ALLOWING FOR RELATED FACTORS

The prevalence of symptoms and diseases in the children was greater in the lower than in the upper social classes and declined with age. Since the proportion of children in social classes I, II, and III (non-manual) was higher among those from homes where electricity was used for cooking (table II) and there were minor differences in age between the two groups of children, it was important to allow for the effect of these factors in the analyses. Moreover, the analysis shown in table I did not take into account the fact that some children had more than one symptom or disease. Fortunately a new computer package—GLIM (Generalised Linear Interactive Models)—which has a facility for fitting log-linear models<sup>11</sup> to frequency data has become available. These models are particularly suitable for analysing the relation between a set of factors and a categorical response when the response cannot be sensibly represented on a quantitative scale. This is a considerable advantage over more commonly used methods, which require the construction of a score, with associated assumptions of normality and the necessity for intervals on the scale to have some quantitative interpretation.

To carry out this analysis we prepared a set of response categories using histories of bronchitis, colds going to the chest, and the three symptoms (day and night cough, morning cough and wheeze). Children reported to have asthma were excluded from the analysis. Although the analysis technique did not require it, we used a sequence of categories related to increasing severity of respiratory illness to simplify the interpretation. Because there was no obviously correct way of doing this we chose the simplest. A count of the positive responses to the five questions on symptoms and diseases was used

to define the following four categories: (1) no symptom or disease; (2) one symptom or disease; (3) two symptoms or diseases; (4) three or more symptoms or diseases.

Since the prevalence of symptoms and disease differed between the sexes, boys and girls were analysed separately. Within each sex the children were divided into eight subgroups, according to social class (II (non-manual) or above; or class III (manual) or below); age (below 8 years; or 8 years and over); and the type of cooking fuel used. Within each subgroup the distribution of the children among the four categories of respiratory illness was determined (table III). These distributions for all the subgroups were then analysed using the log-linear model facility in the general linear model-fitting program<sup>12</sup> to test whether there were systematic and consistent differences between them related to social class, age, or types of fuel. This technique had obvious advantages over the relative-risk approach, with its requirement that the response categories be compressed into a dichotomy, with a consequent loss of information.

As expected, the analyses for both sexes showed that the proportion in the more severe categories of respiratory illness was greater in the lower social class group than the higher group ( $P < 0.03$ ) and greater for younger than for older children ( $P < 0.01$ ). An association between greater severity of illness and the use of gas for cooking was also found after allowing for the effects of social class and age ( $P < 0.07$  for boys;  $P < 0.001$  for girls). In other words, in the gas cooking groups the proportion of children in the more severe illness categories increased at the expense of those in the less severe categories. Thus if girls aged under 8 years and from social class III (manual) or below are taken as an example, 11% of those from homes using electricity had two or more diseases or symptoms compared with 16% of those from homes using gas.

Effects due to latitude and the degree of urbanisation might also have biased the results, so the analysis was extended to include these factors. To represent latitude the areas were grouped into three regions: Scotland, England north of the line joining the Bristol Channel to the Wash, and England south of this line. Urban and rural areas were defined according to whether they had a population density above or below 20 people/hectare. As this extended analysis was too large for our computer facility, urban and rural areas were analysed separately and the respiratory illness categories 3 and 4 combined into one. This also helped to ensure adequate numbers in each category within the 40 subgroups.

Allowing for the effect of these factors in the analysis made no difference to the direction of the relationships of illness severity with age and social class, although the associations did not always reach statistical significance. A relation with latitude did emerge, but this seemed to depend on the degree of urbanisation. For rural areas there was some evidence, confined to girls, that there was more illness in southern England. For urban areas, on the other hand, the proportion of children in the more severe categories was highest in northern England and lowest in the south ( $P < 0.001$  for boys; and  $P < 0.005$  for girls). This finding is difficult to explain simply, although it could be argued that latitude has no effect in rural areas—that is the significant result for the girls was a chance one, while in the urban areas the

TABLE I—Prevalence (%) of respiratory symptoms and diseases during last 12 months in boys and girls according to type of fuel used for cooking in the home

Symptoms and diseases	Boys			Girls		
	Electricity	Gas	P*	Electricity	Gas	P*
Bronchitis	3.1	5.7	<0.001	3.0	4.7	<0.001
Day or night cough	5.4	6.5	<0.001	3.4	5.7	<0.001
Morning cough	3.0	4.3	<0.001	2.0	4.1	<0.001
Colds going to chest	23.0	24.4	<0.002	19.8	24.1	<0.006
Wheeze	10.1	11.2	<0.05	9.7	8.6	<0.005
Asthma	1.8	2.7	<0.02	1.0	1.6	<0.02
No. of children	1645	1274		1556	1240	

\*Probability value for difference between prevalence rates,  $\chi^2$  test.

TABLE II—Distribution of social class in each cooking group

Social class:	I	II	III (non-manual)	III (manual)	IV	V	Total
No. (%) in electricity group	151 (4.7)	576 (18.0)	333 (10.4)	1604 (50.2)	436 (13.6)	100 (3.1)	3204 (100)
No. (%) in gas group	83 (3.2)	319 (12.5)	192 (7.5)	1373 (53.6)	406 (15.9)	181 (7.1)	2554 (100)
No. (%) of children (total)	234 (4.1)	895 (15.5)	525 (9.1)	2977 (51.8)	842 (14.6)	281 (4.9)	5758 (100)

TABLE 11—Percentage of boys and girls classified by respiratory illness category, social class, age, and type of fuel used for cooking in the home

Respiratory illness category <sup>a</sup>	Social classes I-III (non-manual)				Social classes III (manual) + V			
	<8 years		8-14 years		<8 years		8 years	
	Electricity	Gas	Electricity	Gas	Electricity	Gas	Electricity	Gas
<b>Boys</b>								
1	74.4	71.9	70.2	70.1	62.5	75.0	71.0	
2	15.6	14.6	13.1	15.9	17.0	15.7	17.7	
3	4.9	9.0	5.2	3.2	9.4	5.5	6.3	
4	1.0	2.1	2.5	4.2	9.4	7.8	5.0	
Total <sup>b</sup>	100 (201)	100 (185)	100 (165)	100 (180)	100 (375)	100 (309)	100 (675)	100 (654)
<b>Girls</b>								
1	77.6	69.6	61.0	60.4	65.2	66.5	82.2	72.2
2	15.6	17.0	14.2	14.4	21.1	17.5	12.3	16.2
3	4.1	8.9	2.0	5.7	7.4	6.8	9.7	6.6
4	2.1	1.6	1.3	1.1	3.3	4.2	1.8	2.7
Total <sup>b</sup>	100 (171)	100 (112)	100 (101)	100 (167)	100 (343)	100 (317)	100 (674)	100 (623)

<sup>a</sup>See text. <sup>b</sup>Numbers of children are given in parentheses, but they do not add up to 5754 as estimates have been excluded.

effects followed the pattern one might have expected given the more intense industrialisation of the north.

The association between the distribution among the respiratory illness categories and the type of cooking fuel was still apparent even after these extra factors were taken into account. The proportion of children with more than one disease or symptom was still higher among those from homes where gas was used for cooking. But this association was significant only for girls in urban areas ( $P = 0.03$ ); though the trend was in the same direction for both sexes in urban and rural areas. In fact for the girls in rural areas and the boys in urban areas the association was not far from significance ( $P = 0.10$ ).

Although we allowed for the effects of latitude and degree of urbanisation by classifying the areas into six groups, it was still possible that some of the cooking effect could have been explained by the differences between the areas within each group. As it was impractical to divide the children into still more sub-groups we expanded the area groups to 26 at the expense of the respiratory illness categories, which were reduced to two (those with and those without symptoms or diseases). Using a logistic transformation of the proportion of children in the illness categories as the outcome variable, we obtained very similar results to our first log-linear model analysis. After allowing for the effects of social class, age, and area, there was a significant association of symptoms and diseases with the use of gas for cooking in girls ( $P = 0.05$ ), and, although the effect did not reach significance in boys ( $P = 0.30$ ), it was in the same direction.

We also considered other factors that might have affected the comparisons, such as the number of siblings, overcrowding in the home, fuels used for heating and atmospheric smoke and  $SO_2$  levels. Data for these variables were, however, missing for many of the children, so only very small numbers remained within the necessary subgroups. Thus the results from these analyses were not so conclusive and will need confirmation by study of the more complete data now being collected. None the less, when these factors were taken into account, the proportion of children with one or more respiratory symptoms or diseases remained higher in both boys and girls from homes where gas was used. This approached significance in girls ( $P = 0.10$ ), but not in boys.

## Discussion

We have shown that children from homes where gas is used for cooking have a higher prevalence of respiratory symptoms and disease. This may be due to pollution of the indoor atmosphere by the products of gas combustion, but other factors associated with gas cooking and respiratory disease may still underlie the findings. So far as possible we have made allowances for most of the obvious factors. Although the grouping of social class which we had to use was rather broad, the differences in the use of electricity and gas between the social class groups were quite small (table 11). On the other hand, we could not include family smoking habits in the analysis, but the known relation between smoking and social class<sup>19</sup> has allowed us to avoid at least some of the potential bias from this source. It

seems unlikely that within our social class groups there was a higher prevalence of smoking in homes where gas was used for cooking.

The main constituents in the emissions from a gas cooker are  $N_2$ ,  $O_2$ ,  $CO_2$ , and water vapour, with small amounts of  $CH_4$ ,  $C_2H_6$ , and other hydrocarbons,  $CO$ ,  $NO$ ,  $NO_2$ , and various aldehydes. Other pollutants, such as  $HF$ ,  $HCl$ , and  $HBr$ , can be formed as a result of residual aerosol spray vapours in combustion air passing through the flame on the cooker.

Reports<sup>11,12</sup> indicate that the concentrations of oxides of nitrogen emitted from gas cookers are above those recommended in the US Primary Air Quality Standards<sup>10</sup> and Emergency Episode Criteria Guidelines.<sup>11</sup> The maximum level recommended for the annual arithmetic mean is 0.05 ppm, and the alert levels for the 24-hour and one-hour averages are 0.15 ppm and 0.6 ppm respectively. Derwent and Stewart<sup>11</sup> have reported that the concentrations of oxides of nitrogen taken as a whole that are emitted from a gas cooker range from 8 to 33 ppm. Wade *et al.*<sup>12</sup> found that over a two-week period the average concentration of  $NO_2$  in kitchens where a gas cooker was used was over 0.05 ppm, the maximum recommended ambient level. They also showed how the concentration in different parts of the home fluctuated with the use of the cooker, and reached average levels of over 0.15 ppm for two hours in the kitchen.

Little has been published about the effects of these gases on human health. Reports of human exposure have been confined to agricultural and industrial accidents, in which adults have been suddenly exposed to very high levels of  $NO$  and  $NO_2$ , with resulting extensive pulmonary oedema. These levels were much higher than those emitted by gas cookers.<sup>11,12</sup>

Information on the effects on health of low-level exposure to  $NO$  and  $NO_2$  has come from animal and epidemiological studies. Mice have been shown to have an increased susceptibility to infection by *Klebsiella pneumoniae* when first exposed to concentrations of  $NO_2$  of 3.4 to 25 ppm<sup>20</sup> for about two hours. Shy *et al.*, reporting some of the Community Health and Environmental Surveillance System studies,<sup>21</sup> attributed a modest decrease in the respiratory function of children aged 7-8 to exposure to a yearly average concentration of outdoor  $NO_2$  of 0.08 ppm. Their measurements of  $NO_2$  have since, however, been shown to be highly correlated with  $SO_2$  concentrations, and the effects of the two pollutants could not be separated.<sup>22</sup> We have found only one report of studies similar to ours, which were carried out in families living in a suburb of Columbus, Ohio, and on Long Island, New York.<sup>23</sup> In contrast to our findings, the authors found no association between respiratory disease and the use of electricity or gas for cooking.

$SO_2$  is also given off during the burning of gas and is potentially harmful to health. But the sulphur content of gas is legally limited and the levels of  $SO_2$  produced are likely to be very much

2023379628

lower than those currently believed to have adverse effects on health. Thus it seems unlikely that this pollutant would have caused our findings.

Possibly the combustion products of coal gas and natural gas differ in some relevant way. We could not separate the effects of the two types of gas because most of the study areas underwent a changeover from town to natural gas during 1973, and the children were exposed to the products of combustion of both gases.

The relation between gas cooking and respiratory disease seems to be stronger and more consistent for girls than for boys, as would be expected if girls spent more time in the family kitchen. If this is the case, and the difference between the sexes is purely the result of differing exposure, it seems likely that increased ventilation might be sufficient to dispel any risk.

Nevertheless, detailed research is required to determine whether the relation we have found is really due to a direct effect of the products of gas combustion on the respiratory tract before more complicated measures for the protection of health are considered.

We thank Professor Holland as initiator and director of the study for his advice; the trained fieldworkers from St Thomas's Hospital; other members of the study team; and the nurses, teachers, and other assistants in the study areas. We also thank Mr Robert Waller from the MRC Environmental Hazards Unit at St Bartholomew's Hospital Medical School and Dr Stuart Reed from the Scientific Department, County Hall, London for reading the manuscript and giving valuable advice.

## References

- <sup>1</sup> Colley, J. R. T., Douglas, J. W. R., and Reid, D. D. *British Medical Journal*, 1973, 2, 195.
- <sup>2</sup> Reid, D. D., and Fairbairn, A. S. *Lancet*, 1958, 1, 1147.

- <sup>3</sup> Office of Population Censuses and Surveys. *Studies on Medical and Population Subjects No 26. Mortality Statistics from General Practice*. London: HMSO, 1974.
- <sup>4</sup> Office of Population Censuses and Surveys. *Registrar General's Statistical Review of England and Wales for 1973, Part 1. Tables*. Medical London: HMSO, 1975.
- <sup>5</sup> Douglas, J. W. R., and Waller, R. E. *British Journal of Preventive and Social Medicine*, 1969, 20, 1.
- <sup>6</sup> Holland, W. W. *et al.* *British Medical Journal*, 1969, 2, 205.
- <sup>7</sup> Izuz, L. *et al.* *Recent Advances in the Assessment of the Health Effects of Environmental Pollution, Symposium Proceedings*, vol. 1, p. 289. Luxembourg: Commission of the European Communities, 1975.
- <sup>8</sup> Altman, D. G., and Cook, J. *Proceedings of the Royal Society of Medicine*, 1973, 66, 606.
- <sup>9</sup> Office of Population Censuses and Surveys. *Registrar General's Classifications of Occupations, 1970*. London: HMSO, 1970.
- <sup>10</sup> Warren Spring Laboratory. *National Survey of Smoke and Sulphur Dioxide. Instruction Manual*. Stevenage: Warren Spring Laboratory, 1966.
- <sup>11</sup> Plackett, R. L. *Analysis of Categorical Data*. London: Charles Griffin, 1974.
- <sup>12</sup> Seldner, J. A. *Applied Statistics*, 1974, 23, 323.
- <sup>13</sup> Tobacco Research Council. *Statistics of Smoking in the United Kingdom. Research Paper 1*, 7th edn. London: Tobacco Research Council, 1976.
- <sup>14</sup> Derwent, R. C., and Stewart, H. N. M. *Atmospheric Environment*, 1973, 7, 985.
- <sup>15</sup> Wade, W. A., Cole, W. A., and Yarnum, J. E. *Journal of the Air Pollution Control Association*, 1975, 25, 911.
- <sup>16</sup> US Environmental Protection Agency. *Federal Register*, 1971, 36, No 84, Part II, p. 8187.
- <sup>17</sup> US Environmental Protection Agency. *Federal Register*, 1971, 36, No 158, Part II, p. 15503.
- <sup>18</sup> Becklake, M. R., Goldman, H. I., and Freed, C. C. *American Review of Tuberculosis and Pulmonary Disease*, 1957, 76, 398.
- <sup>19</sup> Grayson, R. R. *Annals of Internal Medicine*, 1959, 45, 393.
- <sup>20</sup> Purvis, M. R., and Ehlich, R. *Journal of Infectious Diseases*, 1961, 109, 238.
- <sup>21</sup> Shy, C. M. *et al.* *Archives of Environmental Health*, 1973, 27, 121.
- <sup>22</sup> Warner, P. O., and Stevens, L. *Recent Advances in the Assessment of the Health Effects of Environmental Pollution, Symposium Proceedings*, vol. 1, p. 1001. Luxembourg: Commission of European Communities, 1975.
- <sup>23</sup> Mitchell, R. L. *et al.* *Recent Advances in the Assessment of the Health Effects of Environmental Pollution, Symposium Proceedings*, vol. 2, p. 47. Luxembourg: Commission of European Communities, 1975.

(Accepted 8 June 1977)

# Dextrostix-Eyetone in the insulin hypoglycaemia test

M A PREECE, R G NEWALL

*British Medical Journal*, 1977, 2, 152-154

## Summary

The Ames Dextrostix-Eyetone system was evaluated for monitoring the blood glucose concentration during insulin-induced hypoglycaemia. The results agreed well with laboratory values for plasma glucose, obtained by an orthotoluidine method, and the method was practicable as a bedside technique. In two cases quick results obtained with the Eyetone enabled the insulin tolerance test to be interrupted to prevent severe hypoglycaemia before the clinical indications were obvious. The extra time and effort required were minimal, and its value

seems to far outweigh the disadvantage of the extra work entailed. Nevertheless, care in using the system was important, and the operator must familiarise himself with the system before the most reliable results can be obtained.

## Introduction

The best validated test of pituitary growth hormone (GH) release in man is the insulin tolerance test (ITT), which allows GH and ACTH production by the pituitary to be assessed simultaneously.<sup>1</sup> The test is especially useful as thyrotrophin-releasing hormone (TRH) and gonadotrophin-releasing hormone (GRH) may be given at the same time so that prolactin and gonadotrophin secretion can be assessed simultaneously.

Adequate hypoglycaemia must be achieved before the ITT can be considered to be satisfactorily completed. Hypoglycaemia is generally recognised from the clinical signs (such as sweating) and, retrospectively, by seeing that the plasma glucose concentration has fallen by at least 50% from the fasting value and is below 2.8 mmol/l (50 mg/100 ml) at the nadir.<sup>2</sup> Because of this and of the danger of severe hypoglycaemia, especially in young children, there have been extensive searches for other

Department of Growth and Development, Institute of Child Health, London WC1N 1EH

M A PREECE, MD, MSc, lecturer in child health and growth

Miles Laboratories Ltd, Slough, England

R G NEWALL, MB, FRCS, clinical research associate

2023379629

5

2023379630

Melia, R.J.W., Florey, C.D., Chinn, S. "The Relation between Respiratory Illness in Primary Schoolchildren and the Use of Gas for Cooking I. Results from a National Survey" International Journal of Epidemiology 8(4): 333-338, 1979.

SUMMARY: The relation between the prevalence of respiratory illness and the use of gas for cooking in the home has been investigated in a 5 year longitudinal study of primary schoolchildren from England and Scotland. 4827 boys and girls aged 5 to 10 years from 27 randomly selected areas were examined in 1977, the last year of the study. The prevalence of one or more respiratory symptoms or diseases was higher in children from homes where gas was used for cooking than in those from homes where electricity was used. The association appeared to be independent of age, sex, social class, number of cigarette smokers in the home and latitude but it was only found in urban areas (for boys  $p < 0.005$ ; for girls  $p \leq 0.08$ ). In children aged from 6 to 7 1/2 in 1973 who were followed until the last year of the study there was some indication that the association between respiratory illness and gas cooking may have disappeared as the children grew older. However this trend was not obvious in the other age groups who were followed for 2 to 4 years. The evidence of an association between gas cooking and respiratory illness in 1977 supports results for 1973 presented in an earlier report while the cohort results provide some indication that the association may disappear as children grow older.

2023379631

# The Relation between Respiratory Illness in Primary Schoolchildren and the Use of Gas for Cooking

## I - Results from a National Survey

R J W MELIA, C du V FLOREY and S CHINN

Melia R J W (Department of Community Medicine, St. Thomas's Hospital Medical School, London SE1), Florey C du V and Chinn S. The relation between respiratory illness in primary schoolchildren and the use of gas for cooking. I - results from a national study. *International Journal of Epidemiology* 1979, 8: 333-338.

The relation between the prevalence of respiratory illness and use of gas for cooking in the home has been investigated in a 5 year longitudinal study of primary schoolchildren from England and Scotland. 4827 boys and girls aged 5 to 10 years from 27 randomly selected areas were examined in 1977, the last year of the study. The prevalence of one or more respiratory symptoms or diseases was higher in children from homes where gas was used for cooking than in those from homes where electricity was used. The association appeared to be independent of age, sex, social class, number of cigarette smokers in the home and latitude but it was only found in urban areas (for boys  $p < 0.005$ ; for girls  $p = 0.08$ ). In children aged from 6 to 7½ in 1973 who were followed until the last year of the study there was some indication that the association between respiratory illness and gas cooking may have disappeared as the children grew older. However this trend was not obvious in the other age groups who were followed for 2 to 4 years. The evidence of an association between gas cooking and respiratory illness in 1977 supports results for 1973 presented in an earlier report while the cohort results provide some indication that the association may disappear as children grow older.

We previously reported an association between the prevalence of respiratory symptoms and disease, and the use of gas for cooking using data from a national study of respiratory illness in primary schoolchildren (1). We believed that indoor air pollution from nitrogen dioxide ( $\text{NO}_2$ ) formed during the combustion of gas might have been the cause of this association because this pollutant has been shown to increase susceptibility to respiratory infection in animals (2). In this series of 3 papers we present an analysis of more recent data from our national study and also the results of an investigation of the relation between children's respiratory illness and  $\text{NO}_2$  levels in the home (3, 4).

As the national study was longitudinal and the association had only been reported for children present in the first year, 1973, we examined the

data collected over the 4 following years. Results are reported here for 2 groups of children: those aged 5 to 10 years who were present in 1977 but not 1973 (cross-sectional analysis), and those present in 1973 who were followed-up in subsequent years (cohort analysis). Unlike previous years, in 1977 information was collected on the number of people who smoked cigarettes, cigars and pipes in the home. Additional information was collected on gas water heaters and use of pilot lights on gas cookers as it was thought that these might contribute to the concentration of  $\text{NO}_2$  in the home.

### METHODS

Children aged 6 to 11 years who attended schools in 28 randomly selected areas of England and Scotland were examined annually from 1973 to 1977. The areas were selected from 597 employment exchange areas by stratified random sampling and a socio-economic index was used to obtain a high proportion of poor areas. Details of the method

TABLE 1 Crude prevalence (%) of respiratory symptoms and diseases in boys and girls by type of fuel used for cooking in the home

Symptoms and Diseases	Electricity	Boys Gas	P*	Electricity	Girls Gas	P*
Morning cough	2.1	3.1	<0.20	2.4	3.3	p>0.20
Day or night cough	4.2	6.3	=0.02	4.4	4.7	p>0.20
Wheeze	10.1	10.1	p>0.20	6.2	7.1	p>0.20
Colds going to chest	23.2	26.4	p<0.10	19.6	23.1	p<0.05
Asthma	2.4	2.4	p>0.20	1.0	1.2	p>0.20
Bronchitis	3.2	3.6	p>0.20	2.2	2.4	p>0.20
Any respiratory illness	26.3	31.2	p=0.01	23.1	26.5	p=0.07
No. children	1349	909		1468	901	

\* Probability value of difference between prevalence rates  $\chi^2$  test.

of sampling are described elsewhere (5).

In 1977, however, schools from 4 areas were unable to participate and other state schools in the areas were selected. A further 4 areas declined to take part at all and nearby areas with the same socio-economic index were substituted. One of the new areas was not ready to join the study in 1977 so the children came from 21 English and six Scottish areas. The age range was extended in 1977 to include 5-year olds.

Information about each child and the home environment came from a questionnaire completed by the child's mother or other guardian. Six questions used in the previous years of the study were asked about cough, wheeze, colds going to the chest, and the number of attacks of asthma and bronchitis experienced by the child during the previous 12 months. Other questions were asked about the type of fuels used for cooking and heating in the home, the presence of gas water heaters, the use of pilot lights on gas cookers, and the number of people in the household who smoked cigarettes (at least 5 a day) and cigars or pipes regularly. The father's occupation was coded into social class using the Registrar General's classification (6) and the numbers of bedrooms and people in the household were used to obtain a measure of overcrowding.

#### Population for 1977 Cross-Sectional Analysis

9925 children were included in the study in 1977 but 1330 10 to 11 year olds were excluded because they had also been present in 1973 and we wished to study a different group of children from those among whom the effect of gas cooking had first been found. Out of the remaining 8595, 271 were omitted because their ethnic group was either not

known or known to be non-Caucasian, 88 because their age was not known and 261 because they were aged less than 5. 5008 (63%) of the remaining 7975 children had complete information on the 6 respiratory symptoms and diseases, their father's social class, the number of cigarette smokers in the home and type of fuel used for cooking. 181 of these were excluded because they did not come from homes where only electricity or only gas was used for cooking. As the numbers of cigar and pipe smokers in the home tended to be associated with the number of cigarette smokers we used only the latter in the analysis as a general indicator of smoking in the home. The analysis was carried out on 3017 children from homes with an electric cooker and 1810 from homes with a gas cooker. This 62% sample of the total 7794 children eligible for analysis showed no significant difference in mean height or weight by age from the remaining 38% whose measurements had also been taken. For 2 additional analyses 98% of the 4827 children had information on gas water heaters and 99.6% of those from homes with a gas cooker had data on pilot lights.

#### 1973 Cohort Analysis

Children first examined in 1973 left the study when they left primary school at age 11 or 12, or if they moved away from their area. They could be divided into 5 cohorts according to the number of completed years for which they remained in the study (less than 1 to 4). In our analysis we have considered only children who had been followed-up for at least one year and whose mother had reported the use of the same cooking fuel in each year that their child was studied. There were insufficient numbers for

2023379633



analysis of those who reported a change in cooking fuel. 5758 (73%) of the 7851 Caucasian children aged 6 to 11 years who were included in the study in 1973 had complete information on sex, social class and the 6 respiratory symptoms and diseases, and came from homes where only gas or electricity was used for cooking. Of these 5758, 2408 (42%) had data for full follow-up: 791 children aged 9.5 to 10.9 (14%) were followed up with complete information for one year until 1974, 578 aged 8.5 to 9.4 (10%) until 1975, 502 aged 7.5 to 8.4 (9%) until 1976 and 537 aged 6 to 7.4 (9%) until 1977.

#### CROSS-SECTIONAL RESULTS FROM 1977

##### Crude Prevalences

Only the prevalences of day or night cough in boys ( $p = 0.02$ ) and colds going to the chest in girls ( $p < .05$ ) were found to be significantly higher in children from homes where gas was used for cooking compared with children from homes where electricity was used. Although none of the other symptoms or diseases appeared to have a statistically significant association with gas cooking the prevalences of all symptoms and diseases in girls and of morning cough, colds going to the chest and bronchitis in boys appeared to be higher in children from homes with gas cookers.

As no particular symptom or disease showed a strong association with type of cooking fuel in either sex and the responses to the 6 respiratory questions were inter-related we grouped the various

responses to the 6 respiratory questions by a method similar to that used in our previous paper (1). The children were grouped according to whether they had none, or one or more symptoms or diseases. In both sexes this prevalence was higher in children from homes where gas was used for cooking than in those from homes where electricity was used ( $p = 0.01$  in boys,  $p = 0.07$  in girls).

##### Prevalence and related factors

Several interfering factors needed to be considered in the analysis. The most obvious of these were age and social class (Table 2). Within each age group (less than 8, and 8 or more) and each social class group (I to III (non-manual), and III (manual) to V) the risk of having one or more respiratory symptoms or diseases in homes with gas cookers relative to the risk in homes with electric cookers was greater for all children except girls aged 8 or more from the manual social classes. The weighted relative risk (7) across these groups in homes with gas compared with homes with electric cookers was 1.25 for boys ( $p < 0.05$ ) and 1.19 for girls ( $p = 0.07$ ). The relative risk in boys was similar to that for boys aged 6 to 11 who had been examined in 1973 (1.29,  $p < 0.05$ ) but in girls the relative risk was smaller in 1977 than 1973 when the value was 1.40 ( $p < 0.001$ ).

In addition to age and social class we also considered the number of cigarette smokers in the home. The number of smokers was associated with

TABLE 2 Percentage of boys and girls classified by the number of respiratory symptoms and diseases that they were reported to have, social class, age and type of fuel used for cooking. Risk of having respiratory illness in homes with gas cooking relative to risk in homes with electric cooking also given.

SEX	No. Respiratory Symptoms or Diseases	SOCIAL CLASS: I-III (non-manual)				SOCIAL CLASS: III (manual) - V			
		< 8 Years		> 8 Years		< 8 Years		> 8 Years	
		Electricity	Gas	Electricity	Gas	Electricity	Gas	Electricity	Gas
BOYS	None	72.6	68.3	80.8	71.7	67.2	63.3	76.4	73.1
	1 or more	27.4	31.7	19.2	28.3	32.8	36.7	23.6	26.9
	TOTAL †	100	100	100	100	100	100	100	100
		(277)	(143)	(286)	(113)	(483)	(313)	(301)	(338)
	Relative Risk	1.2		1.7*		1.2		1.2	
GIRLS	None	75.6	72.4	85.2	81.4	72.2	63.7	78.5	81.5
	1 or more	24.4	27.6	14.8	18.6	27.8	36.3	21.5	18.5
	TOTAL †	100	100	100	100	100	100	100	100
		(291)	(134)	(243)	(118)	(497)	(336)	(437)	(313)
	Relative Risk	1.2		1.3		1.5*		0.8	

\*  $p < 0.05$ ; † number of children given in brackets

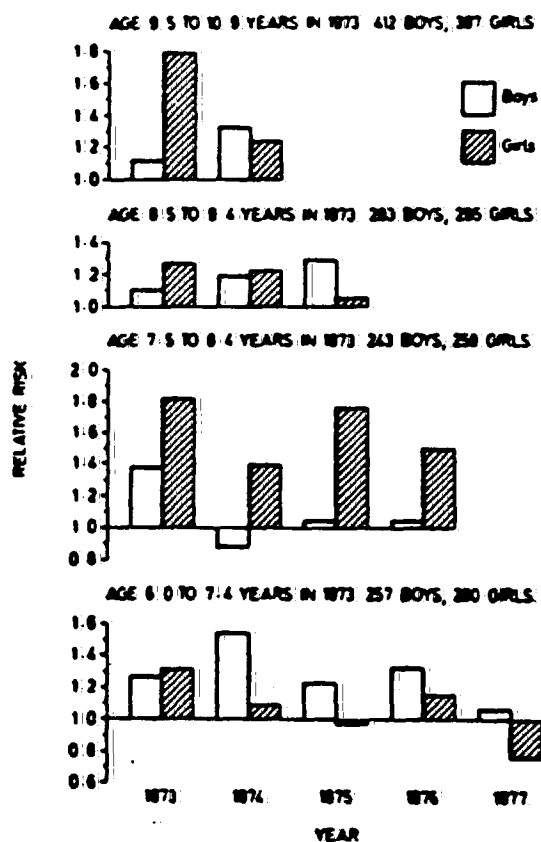


FIGURE  
The relative risk for respiratory illness in children from gas cooking homes compared with children from electric cooking homes is given by sex and year of examination for four cohorts defined by age at entry into the study in 1973.

the use of gas for cooking within manual but not non-manual social classes (Table 3). Furthermore the degree of urbanisation and location of the study areas defined by latitude (Scotland, and England divided into north and south by a line joining the

Bristol Channel to the Wash) were included in the analysis because in 1973 the association between respiratory illness and gas cooking was found to be most consistent in urban areas in the north of England.

The relation between these factors and the prevalence of respiratory illness was examined by fitting a log-linear model using a method of analysis described in greater detail in our earlier paper (1). We first divided the children into 1 of 2 categories according to whether they had none, or one or more symptoms or diseases. We then divided the children by age, sex, social class and type of cooking fuel as shown in Table 2, into rural and urban areas (less than 20, and 20 or more persons per hectare respectively) and the 3 divisions of latitude. The model was fitted separately for boys and girls, and for rural and urban areas as the computer program did not allow space for the full model.

An association between gas cooking and respiratory illness was found independent of the effects of the other factors in urban areas (for boys  $p < 0.005$ , for girls  $p = 0.08$ ) but not rural ones. For girls in rural areas, however, there appeared to be an association in the younger age group. In contrast the effect of number of smokers in the home was only significant in rural (for both sexes  $p < 0.005$ ) but not urban areas. As might have been expected the prevalence was higher in the younger than the older age groups ( $p < 0.05$ ) in all 4 analyses and tended to be higher in the manual than the non-manual social classes although this relation was not always significant. An effect of latitude was only found in girls from urban areas ( $p < 0.05$ ), the prevalence being highest in the north and lowest in the south of England.

We extended the 1977 analysis to allow for the effects of various other factors: overcrowding, type of fuel used for heating in the home and outdoor levels of smoke and sulphur dioxide in each area. Only 1032 boys and 950 girls could be included in

TABLE 3 Percentage of children living in homes with no cigarette smokers and one or more smokers by the father's social class and type of fuel used for cooking in the home.

No. Cigarette Smokers	Social Classes I-III (non-manual)		P	Social Classes III (manual) - V		P
	Electricity	Gas		Electricity	Gas	
None	55.4	58.8		38.3	28.5	
1 or more	44.6	41.2	= 0.20	61.7	71.5	<0.001
TOTAL *	100 (1097)	100 (510)		100 (1920)	100 (1300)	

\* Number of children given in brackets.

## RESPIRATORY ILLNESS IN SCHOOLCHILDREN

337

TABLE 4. Crude prevalence (%) of having one or more respiratory symptoms or diseases in boys and girls by presence of gas water heaters in the home and use of pilot lights on gas cookers.

SEX	Presence of Gas Water Heater			Use of Pilot Light <sup>a</sup>		
	No	Yes	P	No	Yes	P
BOYS†	27.7 (2253)	33.3 (141)	< 0.20	30.8 (305)	31.4 (598)	p > 0.20
GIRLS†	23.9 (2201)	33.9 (121)	< 0.02	23.2 (310)	28.3 (590)	p < 0.15

† number of children given in brackets

<sup>a</sup> children from homes with electric cooking excluded

this analysis so these findings must be treated with caution. However, after allowing for the various effects, respiratory illness was shown to be associated with gas cooking although only significantly so in boys (for boys  $p < 0.02$ ; for girls  $p = 0.15$ ).

Finally we examined the effects of gas water heaters and pilot lights (Table 4) but a relation could only be found between respiratory illness in girls and gas water heaters. When we fitted a log-linear model to include age, social class, and number of smokers in the home in the analysis, the association between water heaters and respiratory illness was inconsistent across the 2 social class and cooking fuel groups. However a significant association was found in girls after allowing for the effects of the other factors ( $p < 0.05$ ).

#### LONGITUDINAL RESULTS FOR 1973 COHORTS

For the 4 cohorts of children who were followed up for 1 to 4 years, the risk of having one or more respiratory symptoms or diseases in homes with gas cookers relative to the risk in homes with electric cookers was calculated for each sex in each year that the children were examined (Figure).

In each cohort in 1973 the risk was greater in homes with gas than homes with electric cookers. In later years, as the cohorts grew older, the relative risk showed considerable variation. Although in most groups the risk was greater in homes with gas than homes with electric cookers, there were groups for whom the risk was either negligible or greater in homes with electric cookers. For each cohort there appeared to be no consistent change in the size of relative risk over time except possibly in the youngest cohort for which the relative risk tended to decline from 1973 to 1977.

#### DISCUSSION

Although the results for the children seen in 1977

were similar in many respects to those for children seen in 1973 there were differences. The effect of gas cooking seemed to be smaller in 1977 than in 1973, at least among girls and, whereas the effect had been most consistent in urban areas in the north of England in 1973, it appeared to be independent of latitude in 1977.

As the prevalences tended to be higher in 1973 than 1977 for children of the same age it is possible that children examined in the first year were predisposed to respiratory illness through the effect of some other factor and were therefore more susceptible to the effect of gas cooking. Differences in weather conditions between the 2 years would not explain these observations as the winter of 1976/77 was colder than that of 1972/73. However as the levels of outdoor air pollution from smoke and sulphur dioxide have been declining over a number of years in the United Kingdom (8) children studied in the first year may have been exposed to higher levels of outdoor air pollution during their lives than children examined in the last year. As the decline in these levels is likely to have been most marked in urban areas in the north of England this may explain why the effect of gas cooking was no longer most consistent in this type of area by 1977. Past high levels of atmospheric pollution may also have contributed to the differences in longitudinal results between the cohorts first examined in 1973.

There seems to be no obvious reason why there should be a gas cooking effect in urban areas and a smoking effect in rural areas. We can only suggest that variation in the size of effects has occurred by chance because the sample of children has been subdivided into so many small groups during the analysis. Similarly, as the effect of gas water heaters was only found in girls, a more thorough investigation would be required before drawing conclusions from this result.

2023379636

In summary we have observed an association between respiratory illness and the use of gas for cooking in 2 separate groups of children seen 4 years apart in our national study. However the relative risk for children in homes with gas cookers compared with those in homes with electric cookers appears to be smaller in 1977, at least in girls, and only significant in urban areas. There is also some evidence that the relative risk may decline as the children grow older.

#### ACKNOWLEDGEMENTS

We are grateful to Professor Holland who initiated and directed the study, and to the Department of Health and Social Security who supplied the grant for our work. We also thank other members of the study team, past and present, including the fieldworkers Ms. Judy Unwin, Ms. Sue Hedges and Ms. Maureen Bufton from St. Thomas's Hospital and the nurses, teachers and other assistants in the study areas.

#### REFERENCES

- (1) Melia R J W, Florey C du V, Altman D G and Swan A V. Association between gas cooking and respiratory disease in children. *British Medical Journal* ii: 149-152, 1977.
- (2) Erlich R, and Henry M C. Chronic toxicity of nitrogen dioxide. I. Effect on resistance to bacterial pneumonia. *Archives of Environmental Health* 17: 860-865, 1968.
- (3) Goldstein B D, Melia R J W, Chinn S, Florey C du V, Clark D and John H II. The relation between respiratory illness in primary schoolchildren and the use of gas for cooking. II. Factors affecting nitrogen dioxide levels in the home. *International Journal of Epidemiology* 8: 339-345, 1979.
- (4) Florey C du V, Melia R J W, Chinn S, Goldstein B D, Brooks A G F, John H H, Craighead I B, and Webster X. The relation between respiratory illness in primary schoolchildren and the use of gas for cooking. III. Nitrogen dioxide, respiratory illness and lung function. *International Journal of Epidemiology* 8: 347-353, 1979.
- (5) Altman D G, and Cook J. A nutritional surveillance study. *Proceedings of the Royal Society of Medicine* 66: 696-697, 1973.
- (6) Office of Population Censuses and Survey, Registrar General's Classifications of Occupations, 1970. HMSO, London, 1970.
- (7) Armitage P. Statistical Methods in Medical Research: 4th Edition, p 427-433. Blackwell, Oxford, 1977.
- (8) Weatherley M L, P M, Gorriah B D and Charnock J. Fuel consumption, smoke and sulphur dioxide emissions and concentrations, and grit and dust deposition in the UK, up to 1973-74. LR 214(AP), Warren Spring Laboratory, Stevenage, 1976.

(Received 6 August 1979)

2023379637

6

2023379638

Speizer, F.E., Ferris, B., Bishop, M.M., Spengler, J. "Respiratory Disease Rates and Pulmonary Function in Children with NO<sub>2</sub> Exposure" American Review of Respiratory Disease 121(1): 3-10, 1980.

SUMMARY: As part of a long-range, prospective study of the health effects of air pollution, approximately 8,000 children from 6 yrs to 10 yrs of age from 6 communities had questionnaires completed by their parents and had simple spirometry performed in school. Comparisons were made between children living in homes with gas stoves and those living in homes with electric stoves. Children from households with gas stoves had a greater history of respiratory illness before age 2 (average difference, 32.5/1,000 children) and small but significantly lower levels of FEV<sub>1</sub> and FVC corrected for height (average difference, 16 ml and 18 ml, respectively). These findings were not explained by differences in social class or by parental smoking habits. Measurements taken in the homes for 24-h periods showed that NO<sub>2</sub> levels were 4 to 7 times higher in homes with gas stoves than in homes with electric stoves. However, these 24-h measurements were generally well below the current federal 24-h outdoor standard of 100 ug/m<sup>3</sup>. Short-term peak exposures, which were in excess of 1,100 ug/m<sup>3</sup>, regularly occurred in kitchens. Further work will be required to determine the importance of these short-term peaks in explaining the effects noted.

2023379639

# Respiratory Disease Rates and Pulmonary Function in Children Associated with NO<sub>2</sub> Exposure<sup>1-4</sup>

FRANK E. SPEIZER, BENJAMIN FERRIS, JR., YVONNE M. M. BISHOP, and JOHN SPENGLER

## SUMMARY

As part of a long-range, prospective study of the health effects of air pollution, approximately 8,000 children from 6 yrs to 10 yrs of age from 6 communities had questionnaires completed by their parents and had simple spirometry performed in school. Comparisons were made between children living in homes with gas stoves and those living in homes with electric stoves. Children from households with gas stoves had a greater history of respiratory illness before age 2 (average difference, 32.5/1,000 children) and small but significantly lower levels of FEV<sub>1</sub> and FVC corrected for height (average difference, 16 ml and 18 ml, respectively). These findings were not explained by differences in social class or by parental smoking habits. Measurements taken in the homes for 24-h periods showed that NO<sub>2</sub> levels were 4 to 7 times higher in homes with gas stoves than in homes with electric stoves. However, these 24-h measurements were generally well below the current federal 24-h outdoor standard of 100 µg/m<sup>3</sup>. Short-term peak exposures, which were in excess of 1,100 µg/m<sup>3</sup>, regularly occurred in kitchens. Further work will be required to determine the importance of these short-term peaks in explaining the effects noted.

## Introduction

There is little doubt that NO<sub>2</sub> at high concentration is associated with acute pulmonary edema and death. Silo filler's disease in which farmers are exposed to concentrations of NO<sub>2</sub> in excess of 200 ppm (376,000 µg/m<sup>3</sup>) with a resultant occurrence of acute pulmonary disease and occasionally death was described in the 1950s (1). Farmers surviving such exposures can develop pulmonary fibrosis.

(Received in original form July 2, 1979 and in revised form October 16, 1979)

<sup>1</sup> From the Departments of Physiology, Biostatistics, and Environmental Health Sciences, Harvard School of Public Health, and the Channing Laboratory, Department of Medicine, Harvard Medical School and Peter Bent Brigham Hospital, Boston, Mass. 02115.

<sup>2</sup> Supported in part by grants from the National Institute of Environmental Health Sciences (ES0002, ES01108), Electric Power Research Institute Contract No. RP 1001 EPRI, and EPA Contract No. EP 68-02-3201.

<sup>3</sup> Presented in part at the Symposium on Health Effects of Nitrogen Oxides, ACS/CSJ Chemical Congress 1979, American Chemical Society, Chemical Society of

Japan, Honolulu, Hawaii and at American Thoracic Society Meeting, May 1979, Las Vegas, Nevada.  
<sup>4</sup> Requests for reprints should be addressed to Frank E. Speizer, M.D., Department of Physiology, Harvard School of Public Health, 665 Huntington Ave., Boston, Mass. 02115.

Japan, Honolulu, Hawaii and at American Thoracic Society Meeting, May 1979, Las Vegas, Nevada.

<sup>4</sup> Requests for reprints should be addressed to Frank E. Speizer, M.D., Department of Physiology, Harvard School of Public Health, 665 Huntington Ave., Boston, Mass. 02115.

2023379640

of NO<sub>x</sub> 4 times greater in kitchens of households with gas stoves than in those with electric stoves (5). The NO<sub>x</sub> appears to be produced by the oxidation of NO when natural gas as a fuel for cooking is burned in the atmosphere. The conversion is rapid, and the NO<sub>x</sub> spreads quickly throughout the house. In contrast to the Melia study of children (2), a study of adult women living and working in households with gas stoves compared with those living and working in households with electric stoves did not show increased respiratory disease rates (3).

The results reported here were obtained as part of a long-range prospective study on the health effects of exposure to ambient levels of pollutants resulting from the burning of fossil fuels. In this study, adults between the ages of 25 and 74, selected at random from 6 communities in the eastern United States, are seen every 3 years, and school children (initially seen in grades 1 and 2) are seen annually. This report is based on the initial measurements of pulmonary function and information on respiratory diseases obtained in the children only in the 6 cities and relates these measurements to the potential indoor exposure that these children have received.

#### Methods

**Study design.** A total of 9,280 children participated in the initial surveys. These children represented 12 separate cohorts from 6 cities. Two cities were surveyed for 3 years, and a new group of first-grade school children was added each year. Thus, these cities provided 6 cohorts. Two cities were surveyed for 2 years giving 4 more cohorts, and 2 cities were surveyed once. In all the cohorts, more than 95 % of the children eligible because of their school grade were studied.

Information about the children's exposure was obtained from a questionnaire, completed by their parents, on the type of home-cooking device and home-heating fuel; the presence or absence of air conditioning, and the presence or absence of adult smokers living in the household, as well as requesting permission to perform lung function tests on the children in the schools.

Forced expiratory measurements were performed using a water-filled low-inertia recording spirometer. The children did not wear nose clips and performed the task in a sitting position, but with free movement possible. Each child had a minimum of 5 and a maximum of 8 attempts in an effort to obtain at least 3 acceptable tracings. Forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV<sub>1</sub>) were read from each tracing. Values were corrected to body temperature and pressure saturated with water vapor (BTPS) and summarized as the mean of the 3 best efforts that were within 170 ml of each other. Standing height in stockinged feet and weight were recorded for each child.

There were 8,866 children (95.5 % of the total seen) who were between 6 yrs and 10 yrs of age at the time of their initial survey, but the sample was reduced to 8,120 children by limiting the analyses to white children.

For each child included in the study, the lung function predicted for his or her height was computed from a regression equation determined by using the children studied in the third year of follow-up from 2 of the cities. These children, who were all within the 5 to 95 percentiles for their height corrected for age, were chosen for the standard as they provided sufficient numbers at each year of age between 6 yrs and 10 yrs (6). The difference between the observed lung function and the predicted value was obtained. These residuals were analyzed using standard analysis of variance techniques.

The reported disease rates were analyzed using log-linear models. By this means it was possible to determine significant interactions between disease, age, sex, cohort, city, and home variables. Adjusted rates were computed based on models that included the significant interactions (7).

Information regarding the differences in air quality associated with different cooking devices was obtained by setting up indoor-outdoor monitors in selected households. These households were not necessarily the homes of children in the study, but were selected to be representative of the kinds of living patterns found in each community. The homes were sampled every sixth day for 24 h, and the same time period in each city, May 1977 through April 1978, was used in all analyses. Measurements were carried out by a household sampling unit, which was placed in an "activity room," a room specifically defined as not being the kitchen or bedroom. Mass respirable particulates (mass median diameter of 3.5  $\mu$ m) were collected on millipore filters (8), and NO<sub>x</sub> was collected by a bubbler technique and measured by the EPA Reference Method, a modified sodium arsenite method (9).

The data on air pollution levels were first adjusted to take into account missing values using a linear model for day of observation and site. The influence of home variables was determined by analysis of variance, with appropriate adjustment of the residual degrees of freedom. In one household, instantaneous peak levels of NO<sub>x</sub> were monitored in the kitchen within 3 feet of a gas stove using a chemiluminescence monitor and a continuous recording.

#### Results

**Assessment of exposure to NO<sub>x</sub>.** About half of the homes in all 6 cities had gas cooking stoves, and about half had electric cooking stoves. (Six % of the homes used some other form of cooking device, alone or in conjunction with gas and/or electricity [1.9 %], or else the type of cooking device was not reported [4.1 %].) There were, however, considerable differences between cities (Figure 1). The distribution of the children by home cooking device ranged from a high of 82.2 % gas cooking



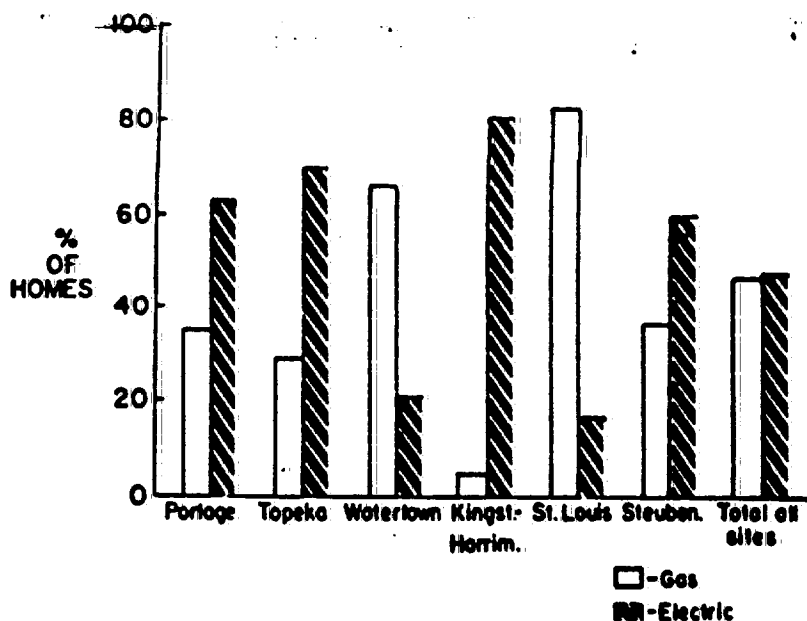


Fig. 1. Percentage of homes with gas or electric stoves, by cities.

stoves in St. Louis to a low of 4.6 % in Kingston-Harriman (figure 1).

Although the number of homes where air quality measurements were made is not large, ranging between 5 and 11 for different cities, the number of 24-h periods for which matched indoor and outdoor data are available is several hundred (table 1). The homes were divided between gas and electric cooking devices, except for Kingston-Harriman where no homes with gas stoves were studied. The results show a gradient of NO<sub>2</sub> levels in homes with electric stoves that reflect outdoor sources of NO<sub>2</sub>. High concentrations in Watertown were presumed to be caused by the proximity of homes, and therefore the monitors, to automobile traffic. A substantial increase in NO<sub>2</sub> levels in homes with gas stoves, except for Steubenville, reflects the addition of indoor sources to the outdoor level of NO<sub>2</sub>. These are 24-h integrated averages collected in an "activity room," but not in the kitchen. In some cities the daily 24-h levels encountered in some households with gas stoves exceeded the federal standard for the annual average of the 24-h NO<sub>2</sub> levels (100 µg/m<sup>3</sup>). Such levels for integrated 24-h values indicated that peak exposures must be substantially higher. This was confirmed in 1 household in which instantaneous monitoring in the kitchen produced peak levels over 1,100 µg/m<sup>3</sup> for short periods of time when the oven was in use and peaks over 500 µg/m<sup>3</sup> when a single gas burner was on (figure 2).

**Health data.** Two sets of data on the children's

health were available: data on previous illnesses reported on questionnaires completed by parents, and data from the current pulmonary function tests. The responses to 3 questions about the previous health of the children were analyzed. The questions asked if there was a history of bronchitis diagnosed by a physician, a history of serious respiratory disease before age 2, and a history of a respiratory illness in the last year.

Both the responses to these questions and the pulmonary function measurements were tested for their relationship to several household variables: type of cooking device, nature of fuel used for heating, presence of adult smokers, presence of air conditioning, and socio-economic status of the family. Socio-economic status included both occupation and educational attainment of the parents.

The 3 reported disease rates were analyzed by fitting log-linear models (7). Two of the variables, type of home-heating fuel and air conditioning, were not related to the disease rates. The social class, parental smoking, and type of cooking stove variables had differing effects on the 3 diseases when each home variable was tested alone (table 2). As the risk factors themselves were inter-related, each disease was evaluated in another log-linear analysis that included these 3 home variables simultaneously. In this multivariate analysis, the effect of the type of cooking stove had a significant association with respiratory disease before age 2, but not with the other 2 reported dis-

2023379642

TABLE 1  
INDOOR AND OUTDOOR 24-H LEVELS OF NO<sub>x</sub> IN 6 U.S. CITIES  
(MAY 1977 TO APRIL 1978)

City	Days (no.)	Home Cooking Units		Geometric Mean Level of NO <sub>x</sub> ( $\mu\text{g}/\text{m}^3$ )				95 Percentile Measured Level of NO <sub>x</sub> ( $\mu\text{g}/\text{m}^3$ ) <sup>†</sup>			
		Elec. (no.)	Gas (no.)	Outdoor		Indoor		Outdoor		Indoor	
				Electric	Gas	Electric	Gas	Electric	Gas	Electric	Gas
Portage*	50	8	3	7.2 (1.55) <sup>‡</sup>	5.9 (1.10)	3.6 (2.13)	14.7 (1.02)	31.8	25.4	17.6	39.3
Topeka	57	6	1	17.5 (1.25)	16.2 —	19.4 (1.26)	31.6 —	42.4	40.7	41.6	73.6
Kingston- Harriman	56	6	—	17.2 (1.25)	—	10.9 (1.43)	—	38.4	—	29.8	—
St. Louis	58	3	6	33.0 (1.17)	37.3 (1.14)	17.1 (2.01)	40.8 (1.42)	64.3	70.9	63.3	79.3
Steubenville	61	2	3	35.7 (1.00)	33.3 (1.35)	21.9 (2.59)	27.4 (2.24)	82.9	87.8	74.5	103.9
Watertown	59	2	5	49.1 (1.42)	49.2 (1.10)	41.43 (1.14)	54.3 (1.21)	101.6	166.3	95.2	116.3

\* Based on 10 month sample

<sup>†</sup> Federal 24 H standard = 100  $\mu\text{g}/\text{m}^3$

<sup>‡</sup> Numbers in parentheses are geometric standard deviations.

cases (table 3). Parental smoking, sex of the child, and city-cohort were not age at the time of reporting. were also associated with respiratory disease before age 2 when other variables were taken into account. Disease rates adjusted for parental smoking, social class, and city-cohort resulted in a difference of 35/1,000 among males and 30/1,000 among females between children in homes with different cooking stoves. Lower rates were found in children of households with electric stoves for each sex in each city-cohort adjusted for parental smoking and social class (figure 3). The effects of parental smoking and city-cohort on respiratory disease before age 2 are not independent, but the

effect of the type of cooking stove appeared to be related to the other home variables.

To assess the effect of home factors on pulmonary function in these children, the difference between the expected and observed FVC and FEV<sub>1</sub> was calculated for each child. The effect of cohort (yr of study and city) and the same home variables on the residual pulmonary function were assessed by analysis of variance. Preliminary regression of lung function on socio-economic status showed no relationship. There was a significant effect ( $p < .01$ ) of cohort on both FEV<sub>1</sub> and FVC. Thus, from city to city and from year to year there were differences in the height-adjusted pulmonary

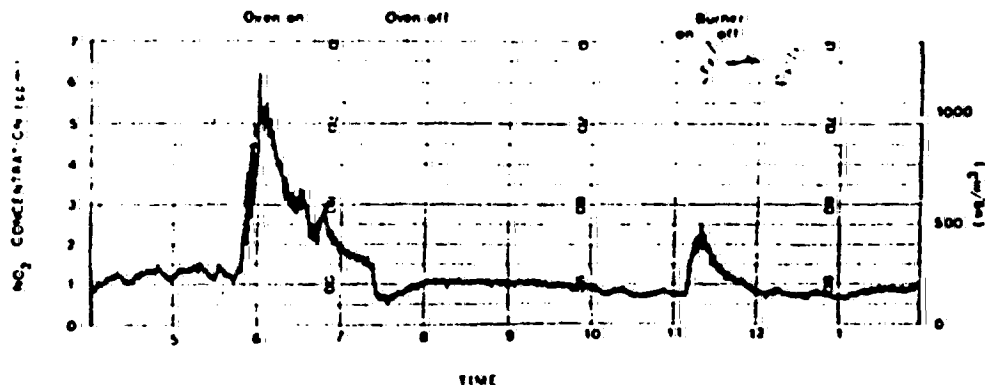


Fig. 2. Instantaneous monitoring of NO<sub>2</sub> in the kitchen 1 meter from gas stove. Numbers along the abscissa represent hrs in the day through 1 P.M. No venting was used.

TABLE 2  
SINGLE FACTOR ODD RATIOS (OR) AND 95% CONFIDENCE LIMITS (CL)  
FOR HOME VARIABLES AND REPORTED DISEASE RATES

		Social Class (Low/High)	Parental Smoking (Some/None)	Home Cooking (Gas/Electric)
History of doctor-	OR	0.97	1.09	0.86
diagnosed bronchitis	CL	.86-1.08	.94-1.26	.79-0.91
Serious respiratory	OR	1.13	1.32	1.12
illness before age 2	CL	1.01-1.26	1.12-1.57	1.00-1.26
Respiratory illness in the	OR	1.13	1.19	0.94
last year	CL	1.05-1.22	1.02-1.39	.86-1.05

function levels in these children, after adjusting for city-cohort effects. There were no significant associations between the presence of air conditioning in the home and lung function measurements (table 4). Although the association between parental smoking and FVC was significant at the 5 % level, with an average range of 15 ml, the result was the opposite of that anticipated, and there was no association between FEV<sub>1</sub> and parental smoking. Home heating and FEV<sub>1</sub> residuals were also significantly associated at the 5 % level. The over-all means covered a 28-ml range and the ordering from low to high was oil, gas, electric.

Although FEV<sub>1</sub> residuals were affected by home heating fuels, the most consistent and significant finding was the lower levels of both FVC and FEV<sub>1</sub> in children whose homes had gas cooking stoves compared with those whose homes had electric stoves. The over-all effect of home cooking, after correcting for cohort effect, was 16 ml and 18 ml, respectively, for FEV<sub>1</sub> and FVC. This effect is apparent in almost all the cohorts. For FEV<sub>1</sub>, in 10 of 12 cohorts, the children in homes with gas stoves had lower function than children in homes with electric stoves (figure 4). For FVC, only 1 of the cohorts (St. Louis, first year), did not show lower levels of pulmonary function in children living in homes with gas stoves compared with those living in homes with electric stoves (figure 4). An unexpected finding in these data

was the low level of pulmonary function measured in Topeka, which is a city with generally lower levels of ambient pollution. In an attempt to investigate this finding, we tested the effect of different interviewers, we reread the spirometer tracings to test the effect of readers, and we compared the values obtained on each spirometer by month of study to test the possibility of a defective machine. None of these tests explained the lower pulmonary function values. In addition, the distribution of height for age of the children in Topeka did not differ significantly from the other cities. We were thus left with the observation that the pulmonary function measurements in the children in Topeka were lower than in other cities and must assume that it was a cohort effect needing further study.

#### Discussion

The significant associations found in this analysis were between home cooking stoves and both illness history and lung function. In addition, there was an association between parental smoking and disease history. The importance of these findings rests with the interpretations of these significant, albeit relatively small, changes. Sufficiently large groups are being studied to observe minor differences between them. The size of the differences found was consistent with the anticipated magni-

TABLE 3  
VALUES OF G\* FOR SPECIFIED DISEASE RATES FOR EACH HOME VARIABLE  
AFTER ADJUSTING FOR THE OTHER TWO HOME VARIABLES

	Social Class		Parental Smoking		Home Cooking	
	G*	p	G*	p	G*	p
History of doctor-diagnosed bronchitis	0.70	NS	1.10	NS	1.90	NS
Serious respiratory illness before age 2	4.12	<.05	10.21	<.01	6.70	<.01
Respiratory illness in the last year	2.12	NS	4.38	<.05	0.14	NS

\* G\* is likelihood statistic derived from the log linear analyses and is distributed, in each case, like a chi square, with 1 degree of freedom.

2023379644

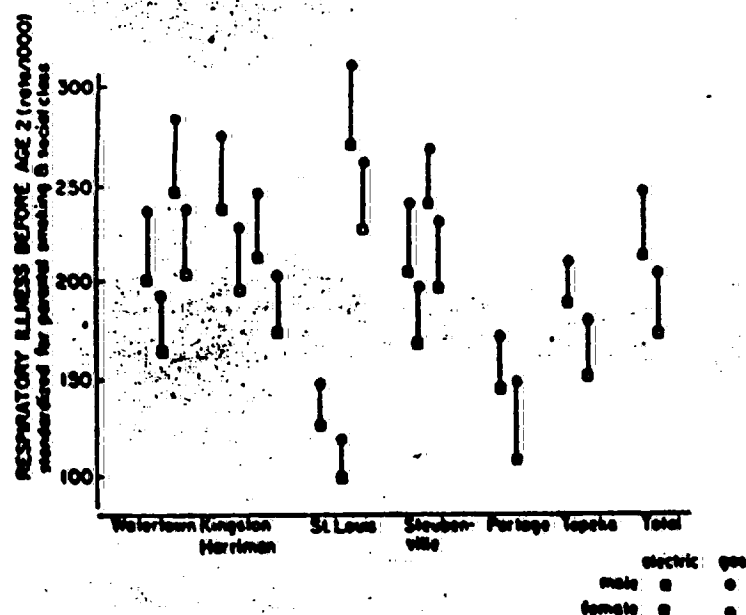


Fig. 3. Respiratory illness before age 2 standardized for parental smoking and social class by cohorts in children 6 to 10 yrs old. Males and females separately by cohort and gas or electric stoves.

tude of effect of environmental agents (11), and the home measurements of air quality are supportive.

The evidence that homes with gas cooking stoves have higher levels of  $\text{NO}_2$  than similar homes with electric stoves has been demonstrated a number of times (4, 5), and peak levels measured over gas stoves have on occasion been re-

ported to reach approximately 1 ppm ( $1,880 \mu\text{g}/\text{m}^3$ ) for periods of 10 to 15 min. This was confirmed in 1 household during continuous monitoring. Similarly we know from both our own investigation and from the studies of Hinds and associates (12) that the mass respirable particulate loads in households with smokers can be several-fold higher than in nonsmoking households.

TABLE 4  
ANALYSIS OF VARIANCE OF CHILDREN'S LUNG FUNCTION FOR HOME VARIABLES  
(CITY-COHORT ADJUSTED)\*

Home Variable	Children (no.)	Lung Function Residuals			
		FEV <sub>1</sub> (liter)	F Ratio	FVC (liter)	F Ratio
Cooking fuel	6,803	—	—	—	—
gas	3,274	-.008	8.11†	-.009	7.94†
electric	3,529	+.008		+.009	
Home fuel	6,734	—	—	—	—
oil	1,419	-.011	3.26†	-.005	0.76
gas	4,432	+.001		-.005	
electric	883	+.017		+.010	
Air conditioning	7,126	—	—	—	—
none	2,855	-.001	0.61	-.002	1.22
partial	2,363	+.003		+.006	
central	1,908	-.003		-.004	
Parental smoking	6,842	—	—	—	—
none	1,724	-.001	.03	-.011	6.28†
some	4,118	+.000		+.004	

\* See text for definition of different cohorts. Largest cohort home variable interaction terms gave F ratios of

1.3, not significant

† p = .01

‡ p = .05

2023379645

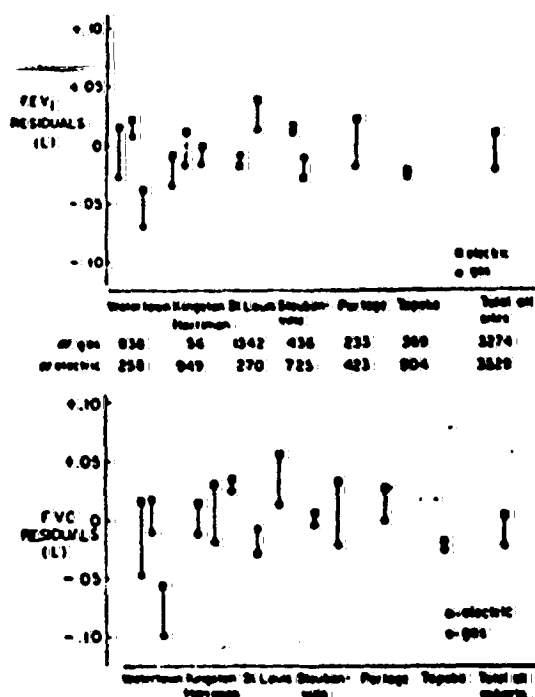


Fig. 4. Forced expiratory volume in 1 s and forced vital capacity residuals by cohort and gas and electric stoves in children 6 to 10 yrs old. (Numbers under the FEV<sub>1</sub> values are the same for FVC values.)

Other factors affecting the association between the disease and either the presence of gas stoves or smoking in the household seem to have been excluded (e.g., socio-economic status, presence of air conditioning, and the type of heating fuel).

In considering the importance of these findings, a number of potential sources of bias must be evaluated. The questionnaire information on disease rates for an individual child depends on the recall ability of the parents, and it may be biased by the present status of the child. The responses also may be biased by the parents' lack of knowledge. No attempt was made to have doctor confirmation of diagnosed disease confirmed independently. It seems unlikely, however, that any biases introduced by these means would be related to the type of home cooking stove consistently for each city and each cohort.

The good response rate, and the sampling plan that ensures that all potentially available children are seen means that the samples are representative of the cities.

The pulmonary function data are potentially subject to different sources of bias than the questionnaire data. These include possible interviewer bias, malfunctioning machine, and biased reading of the spirometer tracing. All these sources of bias have been looked for and have not been found. In

any case, neither the field screeners nor the readers were aware of the individual child's home environment when the spirometry was performed or when the tracings were read. Thus, we cannot attribute any bias to association with home variables.

Essentially, the interpretation of the pulmonary function finding relates to the sensitivity of the measurement and the biologic expectation of the magnitude of anticipated effect in a group of children between 6 yrs and 10 yrs of age. We used FEV<sub>1</sub> as a measure of air flow obstruction in these children, not because we believed it to be the best measure of early obstruction, but because our plan is to follow these children over several years. After several years they will be at a point at which a stable estimate of change in pulmonary function can be related to our understanding of the development of adult obstructive airways disease. In these children, many of whom can empty their entire FVC in less than 2 s, the FEV<sub>1</sub> does not measure obstruction as much as it measures FVC. Thus, it is reassuring to find similar changes in both measures when trying to understand the significance of any given finding.

Our understanding of the biology of lung growth and the nature of the onset of obstructive lung disease in adult life lead us to believe that only minor difference in the rate of functioning lung growth in young children could lead to these children not reaching their full adult lung size. (We are using FVC as a crude indicator of lung size recognizing that the TLC includes not only FVC but also the residual volume, which is not being measured in these field studies.) We do not know whether failure to reach full adult lung size is related to the subsequent susceptibility of developing obstructive lung disease, but it is not an untenable hypothesis that those persons with minor impairment of total lung growth are more susceptible to rapid decline in pulmonary function in adult life (13).

These results differed from those reported in the literature to date only in modest ways. The findings of Melia and co-workers (2) regarding lower respiratory tract illness rates in children whose homes have gas stoves were similar. That study was criticized because it did not have smoking data. In this study the adjustment of rates of illness before age 2 for smoking led to a clear association with gas cooking devices; however, the adjustment of the other 2 historical disease indicators reduced the associations found. The study of Keller and associates (14) of both adults and children in a selected sample of households suggest no association of gas stoves with respira-

2023379646

tory disease rates. This study measured incidence of acute respiratory disease over the course of 1 year; but the number of children studied was quite small and clearly did not represent a general population. Bouhuys and co-workers (15) did study population-based samples of children and adults, but out of the 7,000 persons studied only 165 children between the ages of 7 yrs and 14 yrs were included from the 2 communities under investigation (16). Thus, the fact that they were unable to find an association with home cooking devices may be attributed to the small number studied.

Tager and associates (17), using a different indicator of airways obstruction (mid-maximum expiratory flow), found an association between the pulmonary function levels in children and the number of smokers in the household. No such association using FEV<sub>1</sub> was found in this study. This may mean that the airways obstruction measurement was insensitive.

Further follow-up of these cohorts are underway. Because these data deal with retrospective information, the initial findings reported here need replication to ensure that some subtle bias or alternative explanation for the findings has not been overlooked. If the relative position of these children's lung sizes changes on repeated assessment, it will be important to assess the factors that influence the change. These factors may include changes in ambient pollution (outdoor levels) or changes in personal pollution (indoor exposures and cigarette smoking). In addition, other personal factors such as frequency of respiratory infections, familial history of disease, or other recognized potential risk factors for developing chronic obstructive respiratory disease not discussed in this report will need to be considered.

#### Acknowledgment

The writers would like to thank the local school superintendents, the principals, and the teachers who allowed us into their classrooms; our field teams led by C. Humble, B. Cate, and S. Hancock; D. Dockery for the indoor-outdoor monitoring; our office coordinating staff led by S. Puleo, also J. Weener, M. Eisenstein, and D. Glucksberg for technical computing assistance, and H. Taplin and M. Masters for secretarial and editorial support.

#### References

1. Dowry T, Schuman EM. Silo filler's disease: a syndrome caused by nitrogen dioxide. *JAMA* 1956; 162:153-160.
2. Melia RJW, Florey C Du V, Altman DS, Swan AV. Association between gas cooking and respiratory disease in children. *Br Med J* 1977; 2:149-152.
3. Keller MD, Lanese RR, Mitchell RI, Cote RW. Respiratory illness in households using gas and electricity for cooking. I. Survey of incidence. *Environ Res* 1979; 19:495-503.
4. Melia RJW, Florey C Du V, Darby SC, Palmes ED, Goldstein BD. Differences in NO<sub>2</sub> levels in kitchens with gas or electric cookers. *Atmos Environ* 1978; 12:1379-1381.
5. Wade WA III, Cote WA, Yocum JE. A study of indoor air quality. *J Air Pollut Control Assoc* 1975; 25:933-939.
6. National Center for Health Statistics. The monthly vital statistics report: National Center for Health Statistics Growth Charts. Rockville, MD: National Center for Health Statistics, 1976. (Vital statistics report 25(3), Supplement June 22, 1976.) (DHEW publication [HRA] 76-1120.)
7. Bishop YMSI, Fienberg SE, Holland PW. Discrete multivariate analysis: theory and methods. Cambridge: MIT Press, 1977.
8. Dockery DW, Spengler JD. Personal exposure to respirable particulates and sulfates: measurement and prediction. Chapel Hill: Workshop on the Development and Usage of Personal Exposure Monitors for Exposure and Health Effect Studies, January, 1979.
9. Beard ME, Margeson JH. An evaluation of arsenite procedure for determination of nitrogen dioxide in ambient air. Research Triangle Park, NC: U.S. Environmental Protection Agency, 1974. (EPA-650/4-74-048.)
10. U.S. Environmental Protection Agency. National primary and secondary ambient air quality standards Nitrogen Dioxide Measurement Principle and Calibration Procedure. Fed. Reg. 1976; 41:52686-52695.
11. U.S. Dept. Health, Education, and Welfare. Human health and the environment: some research needs. Washington DC: U. S. Government Printing Office, 1977. (DHEW publication no. NIH 77-1277.)
12. Hinds WC, First MW. Concentrations of nicotine and tobacco in public places. *N Engl J Med* 1975; 292:844-845.
13. Speizer FE, Tager IB. Epidemiology of chronic mucus hypersecretion and obstructive airways disease. *Epidemiologic Reviews* 1979; 1:124-142.
14. Keller MD, Lanese RR, Mitchell RI, Cote RW. Respiratory illness in households using gas and electricity for cooking. II. Symptoms and objective findings. *Environ Res* 1979; 19:504-515.
15. Bouhuys A, Beck GL, Schoenberg JB. Do present levels of air pollution outdoors affect respiratory health? *Nature* 1978; 276:466-471.
16. Mitchell CA, Schilling RSF, Bouhuys A. Community studies of lung disease in Connecticut: organization and methods. *Am J Epidemiol* 1976; 103:212-225.
17. Tager IB, Weiss ST, Rosner B, and Speizer, FE. Effect of parental cigarette smoking on the pulmonary function of children. *Am J Epidemiol* 1979; 110:15-26.

2023379647

7

2023379648

Lebowitz, M.D., Arnet, D.B., Knudson, R. "The Effect Of Passive Smoking On Pulmonary Function In Children" Environment International 8: 371-373, 1982.

The authors of this study conducted an investigation of ventilatory function in 344 nuclear families in a representative population sample in Tucson, Arizona. Household aggregation of body mass was investigated as a possible confounding factor in the reported association between impaired lung function and parental smoking. The authors report that "when household aggregation of body mass was taken into account, there was no relationship of children's pulmonary function values to parental smoking." The study concludes with the statement that "[i]t must be concluded that passive smoking in the family, usually due to parental smoking habits, does not seriously affect permanent markers of respiratory disease such as pulmonary function."

2023379649



## THE EFFECT OF PASSIVE SMOKING ON PULMONARY FUNCTION IN CHILDREN

Michael D. Lebowitz, David B. Arnet, and Ronald Knudson

Division of Respiratory Sciences, Westend Research Laboratories, Arizona Health Sciences Center, Tucson, Arizona 85724, USA

A study of ventilatory function was conducted in 344 nuclear families in a representative community population sample in Tucson, AZ. Household aggregation of pulmonary function, which is dependent on household aggregation of body mass, might affect the relationship of children's pulmonary function to parental smoking. When household aggregation of body mass was taken into account, there was no relationship of children's pulmonary function values to parental smoking. The trend, in the opposite direction, was similar to that found by Speizer *et al.* (1980a), but was not significant in this study. It must be concluded that passive smoking in the family, usually due to parental smoking habits, does not seriously affect permanent markers of respiratory disease such as pulmonary function.

### Introduction

There has been some controversy surrounding the issue of whether passive smoking in households affects the respiratory health of children (NRC, 1981). Some investigators have reported that childhood symptom rates appear related to parental smoking, whereas others disagree. However, it is better to utilize pulmonary function to determine this effect, inasmuch as symptom reporting may show tendencies for parental biases (Cederlof and Colley, 1974; Lebowitz and Burrows, 1976; Schilling *et al.*, 1977). One study by Tager *et al.* (1979) showed the effect of parental smoking on FEV<sub>1</sub>, utilizing Z scores. A similar analysis from the same laboratory in six other, different populations (Speizer *et al.*, 1980a) showed opposite results. Tager *et al.* (1976) also showed that there was household aggregation of pulmonary function values, which might influence such a relationship. This study has demonstrated the relationship of active smoking to ventilatory impairment (Knudson *et al.*, 1976; Burrows *et al.*, 1977), as has been found by others.

This paper attempts to examine the effects of parental smoking on children's pulmonary flow and volumes after correcting for any familial aggregation of ventilatory function and body size.

### Methods

The Tucson Epidemiological Study of Airways Obstructive Diseases, which provided the data base for

these analyses, has been described previously (Lebowitz *et al.*, 1975). Briefly, it is a multistage stratified cluster sample of white non-Mexican-Americans in the Tucson area, where stratification was on age of head of household and on social status. Of the 1655 families studied (approximately 3800 individuals), families with children biologically related to the parents were chosen; these represented 344 households and about one-half of the population (1400). In the first year of this study (1972-1973), pulmonary function tests had been satisfactorily completed on over 90% of those age 6 and over using techniques previously described (Knudson *et al.*, 1976). Smoking habits in adults have been described previously (Burrows *et al.*, 1977); they are similar to those found elsewhere and cover the whole range of amount and duration of smoking.

These nuclear families were divided also into parent-child, spouse, and sibling pairs, the former using oldest children, by sex. Z scores [standard normal deviates  $Z_i = (x_i - \bar{x})/s$ , for  $i$  individuals and  $j$  age-sex groups] were calculated for forced vital capacity (FVC), forced expiratory volume in one second (FEV<sub>1</sub>), maximum flow at 50% of the vital capacity ( $V_{50\%}$ ), and maximum flow at 75% of the expired vital capacity ( $V_{75\%}$ ), within each sex-age group represented in the parent-child pairs. The Z scores were used in analyses of variance to correct for genetic components of body mass in pulmonary function parameters and to detect relationships between parental smoking and children's pulmonary function.

Most houses in this study, as determined by survey, are 1800-2400 ft<sup>2</sup>, not more than 20 years old, have typical 8 ft ceilings, have screened windows, and have central heating and air cooling (usually with filters for both systems). They are kept relatively closed in summer and winter, but are somewhat more open in spring and fall. Air exchange rates have not been measured in this study, but are estimated using published information (NRC, 1981) at between 0.4 and 2.0 per hour, depending on season and use of forced air systems. Indoor pollutant levels were not measured in all of these houses as part of this study. Infiltration of suspended particulate has been measured in about 41 houses (Lebowitz *et al.*, 1982) and is low, though indoor generations is not. Carbon monoxide (CO) indoors and out has been also measured (Lebowitz *et al.*, 1982) and are low as well. The use of types of stoves has been measured in only some families (Lebowitz *et al.*, 1982). Outdoor levels of particulate alone are high in this area, but it is a silica quartz particulate. Nitrogen dioxide and CO are variable, but not in excess of NAAQS (Pima County, 1981).

## Results

It was found that there was a household aggregation of pulmonary function values and of body size. Body size is the key determinant of ventilatory function values (Knudson *et al.*, 1976). When the household aggregation of body size was corrected, there was no household aggregation of pulmonary function that was still significant. Therefore, all pulmonary function values were expressed as percent predicted where the children's prediction equations use their own body size values, their age, and the body size values of their parents. Body size values used included height, weight, sitting height, and the ponderal index (H/W 1/3). Parents' pulmonary

function values were expressed as percent predicted, where the prediction equations used their body size values and their ages. Z scores were then calculated from these percent-predicted values for the age and sex groups (see above).

Analyses of parent-child, spouse, and sibling pairs by the smoking habits of the family members did not show any significant correlations of passive smoking with pulmonary function. This was true whether children's smoking or not smoking was accounted for, and was also true regardless of whether the parents had airway obstructive disease or abnormal pulmonary function tests. It was also independent of family size. Analyses of variance were performed for the children's pulmonary function test values by smoking in the household, by whether both parents smoked, or whether the mother smoked, father smoked, or neither. The total number of nuclear families was reduced to 271 when both parents and all the children age 6 and over in the household had satisfactory pulmonary function data. As can be seen in Table 1, none of the results were statistically significant. Analysis by amount of parental smoking yielded similar results.

In subsequent years of this study, further symptom information and history was collected. Analysis of these data in relation to passive smoking, using previous methods (Lebowitz and Burrows, 1976), indicated no relation to present or past symptoms, including persistent wheeze or early childhood lower respiratory tract illness. Further analysis awaits collection of more longitudinal ventilatory function measurements on the children.

## Discussion

The effects of similar pollutants (specifically NO<sub>x</sub>, CO) from the use of gas stoves on children's and adults'

Table 1. Children's pulmonary function by parental smoking in nuclear families.

Parental Smoking	n	FEV <sub>1</sub> (Z-score) <sup>a</sup>		FVC (Z-score)	
		Mean	SD <sup>**</sup>	Mean	SD
Neither smokes	48	-0.121	0.993	-0.082	0.997
Mother smokes	35	-0.157	0.812	-0.157	0.925
Father smokes	92	-0.042	0.970	-0.059	0.913
Both smoke	96	+0.232	1.059	+0.186	1.062
Total	271	0.026	0.996	0.011	0.988
ANOVA:		p = 0.0796		p = 0.1798	
		V <sub>max</sub> 50% (Z-score)		V <sub>max</sub> 75% (Z-score)	
		Mean	SD	Mean	SD
Neither smokes	48	-0.160	1.194	-0.075	1.058
Mother smokes	35	-0.147	0.848	+0.004	0.888
Father smokes	92	-0.174	0.945	-0.173	1.011
Both smoke	96	+0.150	0.985	+0.202	0.972
Total	271	-0.0002	0.998	-0.0001	0.998
ANOVA:		p = 0.2443		p = 0.072	

<sup>a</sup>See text for explanation.

<sup>\*\*</sup>SD = standard deviation.

2023379651

symptoms and pulmonary function were explored separately, inasmuch as previous studies indicate such potential effects (Speizer *et al.*, 1980b; Comstock *et al.*, 1981). In a substudy, gas stove use was related to acute symptoms only. Analysis in relation to chronic lung disease and ventilatory function had been performed on the total population of 1655 families; gas stove usage was not related to these measures of disease (Lebowitz, 1977). In that same study, it was shown that ambient outdoor particulate matter was slightly related to those measures of disease, but household size and type of house were not (after controlling for socioeconomic status). Socioeconomic status has little independent contribution to pulmonary function (or disease) once more important factors are considered, such as active smoking (Lebowitz, 1982). Thus, these other factors were not part of the analyses reported herein.

It is possible that correction for family body size concordance is not always necessary (Schilling *et al.*, 1977; Speizer *et al.*, 1980a, 1980b). The presence of persistent symptoms, such as wheeze, may be important in some populations (Weiss *et al.*, 1980), but were not in this population. However, consideration of fuel used for heating and cooking is necessary, especially when passive smoke appears important (Speizer *et al.*, 1980a, 1980b; Comstock *et al.*, 1981; NRC, 1981). Results, especially in lower socioeconomic classes or in developing countries, could be misleading otherwise. On the other hand, there still may be an effect of passive smoking, even when accounting for other exposures, in some circumstances and/or some communities, dependent on environmental circumstances, home ventilation factors, and social class.

A more extensive discussion of these factors and their interactions can be found in the National Research Council report (1981) and in an editorial by Frank and Lebowitz (1981).

**Acknowledgement**—This work was supported by NHLBI SCOR Grant No. HL14136.

## References

- Burrows, B., Knudson, R., Cline, M., and Lebowitz, M. D. (1977) Quantitative relationships between cigarette smoking and ventilatory function, *Am. Rev. Respir. Dis.* 115, 195-206.
- Cederlof, R. and Colley, J. (1974) Epidemiological investigations on environmental tobacco smoke, *Scand. J. Respir. Dis. Suppl.* 91, 47-49.
- Comstock, G., Meyer, M. B., Helsing, K. J., and Tockman, M. S. (1981) Respiratory effects of household exposures to tobacco smoke and gas cooking, *Am. Rev. Respir. Dis.* 124, 143-148.
- Frank, R. and Lebowitz, M. D. (1981) The risk of staying in. (Editorial), *Am. Rev. Respir. Dis.* 124, 522.
- Knudson, R. J., Slatin, R., Lebowitz, M. D., and Burrows, B. (1976) The maximum expiratory flow-volume curve: Normal standards variability and the effects of age, *Am. Rev. Respir. Dis.* 113, 587-600.
- Lebowitz, M. D. (1977) The relationship of socio-environmental factors to the prevalence of obstructive lung problems and other chronic conditions, *J. Chron. Dis.* 30, 599-611.
- Lebowitz, M. D. (1982) Multivariate analysis of smoking and other risk factors for obstructive lung diseases and related symptoms, *J. Chron. Dis.* in press.
- Lebowitz, M. D. and Burrows, B. (1976) Respiratory symptoms related to smoking habits of family adults, *Chest* 69, 48-50.
- Lebowitz, M. D., Knudson, R. J., and Burrows, B. (1975) The Tucson epidemiology study of chronic obstructive lung disease. I. Methodology and prevalence of disease, *Am. J. Epidemiol.* 102, 137-152.
- Lebowitz, M. D., O'Rourke, M. K., Dodge, R., Holberg, C. J., Corman, G., Hoshaw, R. W., Pinna, J. L., Barbee, R. A., and Sneller, M. R. (1982) The adverse health effects of biological aerosols, other aerosols, and indoor microclimate on asthmatics and nonasthmatics, *Environ. Int.* 8, 375-380.
- National Research Council (1981) Indoor Pollutants. National Academy of Sciences, Washington, DC.
- Pima County Air Quality Control District (1981) Air Quality in Tucson (AZ). Pima County Government, Tucson.
- Schilling, R. S. F., Letai, A. D., Hui, S. L., Beck, G. J., Schoenberg, J. B., and Bouhuys, A. (1977) Lung function, respiratory disease, and smoking in families, *Am. J. Epidemiol.* 106, 274-283.
- Speizer, F. E., Ferris, B., Jr., Bishop, Y. M. M., and Spengler, J. (1980a) Health effects of indoor NO<sub>2</sub> exposures: Preliminary results, in *Nitrogen Oxides and Their Effects on Health*, S. D. Lee, ed. Ann Arbor Press, Ann Arbor, MI.
- Speizer, F. E., Ferris, B., Jr., Bishop, Y. M. M., and Spengler, J. (1980b) Respiratory disease rates and pulmonary function in children associated with NO<sub>2</sub> exposure, *Am. Rev. Respir. Dis.* 121, 3-10.
- Tager, I. B., Weiss, S. T., Rosner, B., and Speizer, F. E. (1979) Effect of parental cigarette smoking on the pulmonary function of children, *Am. J. Epidemiol.* 110, 15-26.
- Tager, I. B., Rosner, B., Tishler, P. V., Speizer, F. E., and Kass, E. H. (1976) Household aggregation of pulmonary function and chronic bronchitis, *Am. Rev. Respir. Dis.* 114, 485-492.
- Weiss, S. T., Tager, I. B., Speizer, F. E., and Rosner, B. (1980) Persistent wheeze: Its relation to respiratory illness, cigarette smoking, and level of pulmonary function in a population sample of children, *Am. Rev. Respir. Dis.* 122, 697-707.

2023379652



National Institutes of Health, "Report of Workshop on Respiratory Effects of Involuntary Smoke Exposure: Epidemiological Studies", December 1983, pp. 1-11.

SUMMARY: The 1979 Surgeon General's Report on smoking and health presented the available scientific evidence that links involuntary cigarette smoke exposure (passive smoking) to adverse health effects. Existing evidence suggests that children of parents who smoke have more bronchitis and pneumonia during the first year of life and that acute respiratory disease accounts for a higher number of restricted activity days and bed disability days in children whose families smoked than in those whose families did not. In adults, small airway function impairment equivalent to that observed in light smokers has been reported in adults who had never smoked or, lived with smokers but were only exposed to cigarette smoke in the work place. Results such as these need to be confirmed and validated. A number of studies involving large population groups are presently addressing the question of the effect of passive smoking on the respiratory system. However, these studies which are being carried out by at least three different groups, are employing different populations and methodologies and have led to varying conclusions.

An important goal of this workshop was to provide a common forum to these different groups of investigators, along with statisticians conversant with this area, so that the various study designs and results obtained so far could be reviewed in order to identify the probable reasons for differences. Other goals of the workshop were to develop guidelines for collection and analysis of epidemiologic data on the respiratory effects of passive smoking, and to make recommendations for future studies.

The participants included epidemiologists involved in three ongoing population studies of the effect of passive smoking on respiratory health, statisticians, and adult and pediatric pulmonary physicians. The presentations (see Appendix A for agenda) dealt with data from the three groups and methodologic issues relating to data collection and statistical analysis, as well as results of other relevant studies carried out both in the US and other countries. After the first day of formal presentations, the workshop participants (see Appendix B for the list of participants) were divided into smaller task groups, each of which addressed the issues of measuring smoke exposure, outcome variables, confounding variables, other statistical issues related to design and analysis, and the need for additional studies. The following is a summary of the presentations, discussions and recommendations of the task groups.

2023379654

REPORT OF WORKSHOP  
ON  
RESPIRATORY EFFECTS OF INVOLUNTARY  
SMOKE EXPOSURE: EPIDEMIOLOGIC STUDIES

May 1-3, 1983

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service  
National Institutes of Health

December 1983

2023379655

### FOREWORD

On May 1-3, 1983, the Division of Lung Diseases, National Heart, Lung, and Blood Institute sponsored a Workshop on Respiratory Effects of Involuntary Smoke Exposure: Epidemiologic Studies, which was held in Bethesda, Maryland. Twenty-one investigators from the fields of epidemiology, statistics, and adult and pediatric pulmonary medicine participated. This report, prepared by the workshop chairman, session recorders, and Division of Lung Diseases staff, summarizes the presentations and makes recommendations for future studies.

2023379656

## TABLE OF CONTENTS

	<u>Page</u>
I. INTRODUCTION . . . . .	1
II. COMMUNITY-BASED STUDIES ON THE PULMONARY EFFECTS . OF PASSIVE SMOKING . . . . .	2
III. METHODOLOGIC CONSIDERATIONS. . . . .	2
IV. CONCLUSIONS OF WORKING GROUPS. . . . .	4
V. RESEARCH RECOMMENDATIONS . . . . .	6
VI. SUMMARY AND CONCLUSIONS. . . . .	7
VII. APPENDICES	
A. AGENDA . . . . .	8
B. PARTICIPANTS. . . . .	10



## INTRODUCTION

The 1979 Surgeon General's Report on smoking and health presented the available scientific evidence that links involuntary cigarette smoke exposure (passive smoking) to adverse health effects. Existing evidence suggests that children of parents who smoke have more bronchitis and pneumonia during the first year of life and that acute respiratory disease accounts for a higher number of restricted activity days and bed disability days in children whose families smoked than in those whose families did not. In adults, small airway function impairment equivalent to that observed in light smokers has been reported in adults who had never smoked or lived with smokers but were only exposed to cigarette smoke in the work place. Results such as these need to be confirmed and validated. A number of studies involving large population groups are presently addressing the question of the effect of passive smoking on the respiratory system. However, these studies which are being carried out by at least three different groups, are employing different populations and methodologies and have led to varying conclusions.

An important goal of this workshop was to provide a common forum to these different groups of investigators, along with statisticians conversant with this area, so that the various study designs and results obtained so far could be reviewed in order to identify the probable reasons for differences. Other goals of the workshop were to develop guidelines for collection and analysis of epidemiologic data on the respiratory effects of passive smoking, and to make recommendations for future studies.

The participants included epidemiologists involved in three ongoing population studies of the effect of passive smoking on respiratory health, statisticians, and adult and pediatric pulmonary physicians. The presentations (see Appendix A for agenda) dealt with data from the three groups and methodologic issues relating to data collection and statistical analysis, as well as results of other relevant studies carried out both in the US and other countries. After the first day of formal presentations, the workshop participants (see Appendix B for the list of participants) were divided into smaller task groups, each of which addressed the issues of measuring smoke exposure, outcome variables, confounding variables, other statistical issues related to design and analysis, and the need for additional studies. The following is a summary of the presentations, discussions and recommendations of the task groups.

2023379658

## COMMUNITY-BASED STUDIES ON THE PULMONARY EFFECTS OF PASSIVE SMOKING

Findings from community studies of the effect of passive smoking on the respiratory system were summarized. These presentations included data from populations in East Boston, Massachusetts, the Six Cities Study, Tucson, Arizona, and Tecumseh, Michigan. Although none of these studies were originally designed to address the question of the effect of passive smoking on the respiratory system, all have succeeded in obtaining a considerable amount of relevant data.

The methods of data collection and data analysis are somewhat different from group to group, and the results and conclusions of the studies also showed differences. All of the studies have been using questionnaires to assess exposure and symptom prevalence and, in general, the one second forced expiratory volume ( $FEV_1$ ) has been used as the lung function outcome variable of interest.

Most of the available data that have been analyzed are cross-sectional in nature; longitudinal data from a cohort followed for seven years in East Boston, Massachusetts, have been published since the workshop. In the cross-sectional community-based population studies, the effect of passive smoking on lung function varied from none to a very small effect (0 - 3% loss in  $FEV_1$ ). In the longitudinal study, a measurable effect on the development of pulmonary function was seen in the children with a mother who smoked throughout the child's life. Whether this reflects a postnatal effect of passive smoking on lung growth and development, an in utero effect or an effect on bronchial reactivity such that some individuals exposed to passive smoking develop an increase in bronchial reactivity, an increase in mucus in the airways, increased susceptibility to lower respiratory tract infection or some other as yet undefined effect is not yet clear. Better measures of exposure, more longitudinal data and more information about bronchial reactivity are needed before this can be resolved. Better measures of exposure will probably involve biological monitoring, for example, the measurement of cotinine in biological fluids such as saliva and urine. The size and complexity of the data sets accumulated in these population based studies have necessitated the development of new analytical techniques and the adaptation of existing techniques to apply to both cross-sectional and longitudinal data.

## METHODOLOGIC CONSIDERATIONS

The relatively small differences in the effects found in the various studies discussed at this workshop may be real and represent true differences among the various communities studied in the measurable effect of involuntary smoke exposure. Such differences may be caused by regional and geographic

2023379659

variations in levels of indoor air pollution that might result from differences in housing - (e.g., well insulated versus poorly insulated houses,) and life style (e.g., predominantly indoor living versus predominantly outdoor living.) On the other hand, the differences may also be due to methodologic differences in data collection and/or analysis and in the way in which potentially confounding variables have been handled.

The difficulty of controlling for potentially confounding variables was recognized. Such variables include: 1) unvented combustion products from different kinds of stoves used for both heating and cooking, e.g., gas, wood and kerosene, 2) other indoor pollutants such as formaldehyde and respirable particulate matter, 3) indoor pollutants of organic origin such as pollens, molds, mites, other allergens and infectious organisms, 4) characteristics of indoor environments such as temperature, humidity, and frequency of air exchanges, 5) socio-economic status, culture (ethnic), and such factors as crowding, number of siblings, household conditions, child care, reporting biases, etc., 6) demographic and medical characteristics of the study population such as age, sex, marital status, the presence of underlying respiratory conditions, atopy, infections, disability and/or co-morbidity, 7) parental symptoms such as productive cough which will affect reporting, 8) maternal smoking during pregnancy, 9) annoyance responses and other psychological or social responses to tobacco smoking in a nonsmoker. Extensive as this list of potentially compounding variables may be, the importance of taking them into consideration in the study design and analysis cannot be overemphasized.

Given the complexity and number of the potentially confounding variables, the importance of analyzing all the data sets using a common statistical approach was recognized. Also, the importance of distinguishing a statistically significant difference between groups from a clinically significant difference was emphasized. In this regard, a small difference (e.g., 1-3% in FEV<sub>1</sub>) in a cross-sectional study between children from homes in which one parent smoked and those from homes in which no one smoked, might be statistically significant but not be of any clinical significance. On the other hand, a 7% difference in rate of increase in FEV<sub>1</sub> over 7 years observed longitudinally may be both statistically and clinically significant. It is therefore important to use outcome variables (such as FEV<sub>1</sub>) which are of clinical importance rather than using other lung function tests which are extremely sensitive. Likewise, longitudinal data are generally more useful and informative than cross-sectional data.

Many of the differences among the many population studies which have looked at the effect of active and passive smoking on the lung function may be attributable to exposure and/or dose. The logistical difficulties in adequately monitoring these variables are recognized as is the need to develop techniques which are able to measure the biological burden of tobacco smoke. In the future it is likely that considerably less attention will be paid to indirect measures of exposure such as area and personal samplers and more attention paid to biological markers of exposure.

2023379660

#### IV

#### CONCLUSIONS OF WORKING GROUPS

##### A. Study populations

None of the population studies already under way was designed specifically to look at the effect of passive smoking on the respiratory system. However, if the results from these studies show consistency, it may be possible to arrive at answers to most of the questions about the effects of passive smoking on the lungs. Existing data sets should be analyzed and the results compared before any further studies are designed to address this question. An exception to this might be for the age group 0-5 years for which there is very little existing information or planned study because of the difficulties inherent in obtaining accurate measures of lung function in this age group. Also of particular interest are the changes taking place in lung function during the transition between the late teen years and early twenties and the decline in lung function in early adult life. There is presently insufficient information about the possible effect of risk factors such as passive smoking on this transition phase. Another area of particular interest is the occupational setting. It may be that passive smoking is more hazardous in certain occupational settings than in others.

##### B. Outcome Variables

The usual measures of outcome that are presently employed are 1) some measure of lung function and 2) questionnaire information. Every attempt should be made to obtain information in a standardized fashion, (as is presently being done in most of the ongoing studies). Since there are differences of opinion as to which measure of volume or flow should be regarded as the "best" measurement, it is recommended that the complete flow-volume or volume-time curves should be saved. In addition, more attention should be paid to obtaining information about airway reactivity since the existing evidence suggests that exposure to passive smoking may alter an individual's airway reactivity. Also, there is an urgent need to develop pulmonary function tests for use in very young children (below five years), with particular attention to linking these tests with those for older age groups.

Most groups are presently using the standardized ATS-DLD respiratory symptom questionnaire to define symptoms and disease states. It should be noted that this questionnaire was developed to define disease states such as chronic bronchitis and, therefore, may not be entirely suitable to elicit the symptoms associated with passive smoking. Likewise, the pediatric questionnaire was not developed with the idea of identifying symptoms associated with passive smoking. It is recommended, therefore, that new questions should be designed to add to both the adult and the pediatric question-

2023379661

naires to obtain information, in a standardized fashion, about involuntary smoke exposure.

C. Measurement of Dose/Exposure

Lack of proper attention to the estimation or measurement of exposure is a major weakness of all the studies carried out so far. Direct measurement of exposure to tobacco smoke and other combustion products is, at present, too difficult to consider in population studies. It is possible, however, to significantly improve our estimates of exposure. This can be done by developing standardized questions for characterization of indoor sources of pollution, including smoking and by using passive monitors to estimate average ventilation within buildings. Probably most important is the evaluation of biological monitors, in particular, urinary and salivary cotinine levels as indicators of levels of exposure to tobacco smoke.

D. Confounding Variables

There are many potential confounding variables which must be taken into account. Data on these variables are not presently being collected uniformly among the studies underway. It is hard to recommend any specific strategy with regard to confounders, but it must be emphasized that any study which ignores them will be seriously flawed. A list of potentially confounding variables is provided in Section III.

Atopy is important to measure, but cannot be determined by questionnaire data. Only skin tests and IgE measurements are appropriate at present. The development of a standardized approach to measuring the atopic status of an individual should be undertaken.

E. Other statistical issues in design and analysis

The investigators agreed that the various study groups should attempt to cross validate results using analytic techniques from other studies on their own data. Existing statistical methods plus the adaptations of existing methods that have been developed provide a good starting place. In certain instances new methods will still need to be developed. For each study and data set, it is important to place confidence limits on the results, evaluate them in the light of possible biases specific to that study and interpret the results in terms of whether they are clinically and biologically meaningful as well as statistically significant.

F. Additional studies

The participants concluded that the existing studies and data sets should be explored extensively and the results of the various studies compared in order to see if an agreement on the effect of passive smoking on the respiratory system may be reached by the various investigators. Following such an analysis, it will probably be clear as to whether new studies need to be designed to answer specific questions.

It may also be worthwhile to explore other existing data sets which may have obtained information about exposure to passive smoking such as MRFIT, Framingham, the UK National Birthday study (1952), the Japanese (Hirayama) data set and French (Kauffman) data sets.

One area that does need additional study is the development and testing of better measures of involuntary smoke exposure, such as area and personal air samplers and biological markers of exposure. For example, salivary and urinary cotinine levels. These need to be non-invasive.

## V

### RESEARCH RECOMMENDATIONS

#### A. Available data

1. The groups with ongoing studies should be encouraged to use common methods of analysis in addition to any methods they are already employing.
2. The use of standardized methods for obtaining questionnaire and lung function data should be continued. However, questionnaires specifically designed to define disease or symptoms in smokers may not be adequate and new questions capable of eliciting more subtle responses are needed.
3. Where possible, a measure of bronchial reactivity and a measure of an individual's atopic status using skin tests and serum IgE should be included.
4. All possible confounding variables need to be taken into account in any analyses.
5. Measures of exposure such as salivary and urinary cotinine ought to be obtained to validate questionnaire results.

#### B. New Studies

1. Additional studies are probably required in young children (below five years) to obtain more information about the relationship between passive exposure to tobacco smoke and the incidence of lower respiratory tract infections, the development of symptoms, lung growth and lung function.
2. Improved methods of measuring exposure to both tobacco smoke and other indoor pollutants need to be developed and validated. An example of this is the use of salivary and urinary cotinine.

2023379663

## SUMMARY AND CONCLUSIONS

A review of the data from the studies which have been carried out or are in progress which address the effect of passive smoking on the respiratory system suggests that the effect varies from negligible to quite small. From this review, it was not possible to determine whether there is a specific group which is at increased risk or what the mechanism of the effect (if any) may be. The data sets which already exist and are presently being collected are large and complex and, not surprisingly, there are differences, although small, in the results, among the data sets discussed at this workshop. These differences may be due to real differences among the populations being studied or may be due to methodologic differences that inevitably occur from study to study, both in the data collection and analysis. A common approach to the analysis may help to answer this question. It seems likely that the existing data sets contain sufficient information to allow some conclusions to be reached on the effect of passive smoking on the respiratory system. New large scale population studies (of subjects above 5 years of age) should probably not be initiated until the existing data sets have been thoroughly evaluated. There is, however, an urgent need for the development and evaluation of non-invasive biological markers of exposure.

APPENDIX A  
DIVISION OF LUNG DISEASES  
WORKSHOP ON RESPIRATORY EFFECTS OF INVOLUNTARY SMOKE EXPOSURE:  
EPIDEMIOLOGIC STUDIES

May 1-3, 1983

Chairman: Sonia Buist

May 1

Welcome  
Smoking and Pulmonary Health - Goals of Workshop  
Pulmonary Effects of Passive Smoking

S. Hurd  
S. Buist  
C. Rossiter

May 2

COMMUNITY BASED STUDIES ON THE PULMONARY EFFECTS OF  
PASSIVE SMOKING

Moderator: S. Buist

Studies from Boston, Massachusetts

I. Tager  
F. Speizer  
S. Weiss  
D. Dockery  
B. Ferris  
B. Rosner  
T. Louis

Studies from Tucson, Arizona

B. Burrows  
M. Lebowitz  
L. Taussig

Studies from Ann Arbor, Michigan

M. Higgins  
I. Higgins  
J. Keller  
A. Monto

OTHER STUDIES AND METHODOLOGICAL ISSUES

Moderator: H. Weill

WHO Studies

M. Lebowitz

Measurement of Indoor Pollution

J. Stolwijk

2023379665



May 3

GROUP DISCUSSIONS TO DEVELOP RECOMMENDATIONS  
ON THE FOLLOWING ISSUES

Exposure Measures

Outcome Variables

Confounding Variables

Other Statistical Issues in Design  
and Analysis

Additional Studies

FINAL PRESENTATIONS AND RECOMMENDATIONS

Moderator: S. Buist

SUMMARIES OF GROUP DISCUSSIONS

RECOMMENDATIONS FOR FUTURE RESEARCH

CONCLUDING REMARKS

2023379666

## APPENDIX B

### PARTICIPANTS

Sonia Buist, M.D.  
Professor of Medicine  
and Physiology  
The Oregon Health Sciences  
University  
School of Medicine  
3181 SW Sam Jackson Park Road  
Portland, OR 97201

Benjamin Burrows, M.D.  
Professor of Internal Medicine  
Division of Respiratory Sciences  
The University of Arizona Health  
Sciences Center  
1501 North Campbell Avenue  
Tucson, AZ 85724

John E. Diem, Ph.D.  
Professor of Statistics  
Program in Applied Statistics  
Tulane University  
424 Gibson Hall  
New Orleans, LA 70118

Douglas Dockery, D.Sc.  
Research Associate  
Department of Physiology  
Building 1, Room 1416  
Harvard School of Public Health  
665 Huntington Avenue  
Boston, MA 02115

Benjamin Ferris, Jr., M.D.  
Professor of Environmental Health  
and Safety  
Department of Physiology  
Harvard School of Public Health  
665 Huntington Avenue  
Boston, MA 02115

Ian Higgins, M.D.  
Professor of Epidemiology  
University of Michigan  
School of Public Health  
109 Observatory Street  
Ann Arbor, MI 48109

Millicent Higgins, M.D., D.P.H.  
Professor of Epidemiology  
University of Michigan  
School of Public Health  
109 Observatory Street  
Ann Arbor, MI 48109

Jacob Keller, MPH  
Senior Research Associate  
University of Michigan  
School of Public Health  
109 Observatory Street  
Ann Arbor, MI 48109

Michael D. Lebowitz, Ph.D.  
Professor of Internal Medicine  
Division of Respiratory Sciences  
The University of Arizona Health  
Sciences Center  
1501 North Campbell Avenue  
Tucson, AZ 85724

Thomas Louis, Ph.D.  
Associate Professor  
Harvard University  
School of Public Health  
Department of Biostatistics  
677 Huntington Avenue  
Boston, MA 02115

Arnold S. Monto, M.D.  
Professor of Epidemiology  
University of Michigan  
School of Public Health  
109 Observatory Street  
Ann Arbor, MI 48109

Bernard Rosner, Ph.D.  
Associate Professor of Preventive  
Medicine and Clinical Epidemiology  
Channing Laboratory  
180 Longwood Avenue  
Boston, MA 02115

2023379667

Charles E. Rossiter  
Clinical Research Center  
Division of Computing and Statistics  
Watford Road, Harrow, Middlesex  
England HA1 3UJ

Frank E. Speizer, M.D.  
Associate Professor of Medicine  
Harvard Medical School  
Channing Laboratory  
180 Longwood Avenue  
Boston, MA 02115

Jan A. J. Stolwijk, Ph.D.  
Chairman, Department of  
Epidemiology and Public Health  
Yale University School of Medicine  
P.O. Box 3333  
60 College Street  
New Haven, CT 06510

Ira B. Tager, M.D.  
Assistant Professor of Medicine  
Beth Israel Hospital  
330 Brookline Avenue  
Boston, MA 02215

Lynn M. Taussig, M.D.  
Professor, Department of  
Pediatrics  
The University of Arizona Health  
Sciences Center  
1501 North Campbell Avenue  
Tucson, AZ 85724

Division of Lung Diseases Staff  
National Heart, Lung, and Blood Institute

Suzanne S. Hurd, Ph.D.  
Acting Director

J. Sri Ram, Ph.D.  
Chief, Airways Diseases Branch

Zakir H. Bengali, Ph.D.  
Airways Diseases Branch

Hannah H. Peavy, M.D.  
Airways Diseases Branch

Mike Wall, M.D.  
Assistant Professor of Pediatrics  
Division of Chest Diseases  
The Oregon Health Sciences  
University  
School of Medicine  
3181 SW Sam Jackson Park Road  
Portland, OR 97201

Hans Weill, M.D.  
Professor of Medicine  
Tulane University School of Medicine  
1700 Perdido Street  
New Orleans, LA 70112

Scott T. Weiss, M.D., M.S.  
Associate Chief, Pulmonary Unit  
Beth Israel Hospital  
330 Brookline Avenue  
Boston, MA 02215

Margaret Wu, Ph.D.  
Biometric Research Branch,  
Division of Heart and Vascular  
Diseases  
National Heart, Lung, and Blood  
Institute  
Bethesda, MD 20205

2023379668

**2023379669**

Ekwo, E.E., Weinberger, M.M., Lachenbruch, P.A., Huntley, W.H.  
"Relationship of Parental Smoking and Gas Cooking to Respiratory  
Disease in Children" Chest 64: 662-668, 1983.

SUMMARY: In a survey of 1,355 children six to 12 years of age, the risk of hospitalization for respiratory illness among children before age two years was increased when gas was used for cooking at home ( $p < 0.001$ ) or at least one of the parents smoked ( $p < 0.02$ ). The occurrence of cough with colds in children was also significantly increased when one or both parents smoked ( $p < 0.001$ ). Small but significant increases ( $p < .05$ ) in the mean values of forced expiratory volume at one second, the flow rate of 75 percent of the forced vital capacity, and the forced expiratory flow rate from 25 percent to 75 percent of the vital capacity (FEF 25-75) were seen after administering inhaled isoproterenol to children whose parents smoked ( $n = 94$ ) but not among children whose parents did not smoke ( $n = 89$ ); this was not seen in association with gas cooking. Thus, exposure of children during the first two years of life to gas cooking or cigarette smoking appears to be associated with an increased risk of hospitalization for respiratory illness, and cigarette smoking appears to be associated with a more consistent response to inhaled bronchodilator among six - to 12-year-old children with no other history of chronic respiratory illness.

2023379670

# Relationship of Parental Smoking and Gas Cooking to Respiratory Disease in Children\*

Edem E. Ekwo, M.D., M.P.H.; Miles M. Weinberger, M.D., F.C.C.P.;  
Peter A. Lachenbruch, Ph.D.; and William H. Huntley, R.R.T.

In a survey of 1,355 children six to 12 years of age, the risk of hospitalization for respiratory illness among children before age two years was increased when gas was used for cooking at home ( $p < 0.001$ ) or at least one of the parents smoked ( $p < 0.02$ ). The occurrence of cough with colds in children also was significantly increased when one or both parents smoked ( $p < 0.001$ ). Small but significant increases ( $p < .05$ ) in the mean values of forced expiratory volume at one second, the flow rate at 75 percent of the forced vital capacity, and the forced expiratory flow rate from 25 percent to 75 percent of the vital capacity (FEF<sub>25-75</sub>) were

seen after administering inhaled isoproterenol to children whose parents smoked ( $n = 94$ ) but not among children whose parents did not smoke ( $n = 89$ ); this was not seen in association with gas cooking. Thus, exposure of children during the first two years of life to gas cooking or cigarette smoking appears to be associated with an increased risk of hospitalization for respiratory illness, and cigarette smoking appears to be associated with a more consistent response to inhaled bronchodilator among six- to 12-year-old children with no other history of chronic respiratory illness.

Parental smoking has been shown to be related to increased risk of respiratory illness in children during the first year of life,<sup>1,2</sup> and to an increased risk of morning cough, respiratory infections, and breathlessness among older children.<sup>3,4</sup> Specifically, an increased incidence of pneumonia and bronchitis with consequent hospitalizations has been reported among infants whose parents smoked compared to children whose parents did not smoke.<sup>1</sup> Parental smoking also

For editorial comment see page 651

has been reported to increase the risk of persistent wheeze<sup>5</sup> and symptomatic asthma.<sup>6</sup> In a study of British secondary schoolchildren that showed early morning cough to be more commonly reported by children who smoked, the effect on these smoking children of parental smoking appeared to be additive.<sup>4</sup> A decrease in pulmonary function measurements also has been noted in nonsmoking children whose parents smoked.<sup>4,5</sup>

An association has been similarly shown between respiratory illness in children and gas cooking, apparently from increased levels of nitrogen dioxide and nitric oxide in the homes with gas stoves.<sup>7,8</sup> In addition, pulmonary function measurements performed in school-age children were found to be lower in association with the use of gas stoves in the home.<sup>8,9</sup>

The current study was designed to further examine

the relationship of parental smoking and gas cooking on the occurrence of respiratory illness and symptoms in children from a midwestern university community. Additionally, we examined the relationship between these environmental exposures and pulmonary functions.

## METHODS

### Subjects

Children, ages 6 to 12, who attended primary school in the Iowa City School District were contacted after permission was obtained from school administrators. The school district serves a university community. The children were therefore generally from middle and upper social classes. Participating schools included approximately 87 percent of the 2,062 children six to 12 years of age enrolled in the school district. Children from the participating schools were sent home with a letter explaining to parents the purpose of the studies, the information we were interested in collecting and why. The parents were requested to complete a modification of the questionnaire developed by the American Thoracic Society (ATS) for the Division of Lung Disease (DLD) of the National Heart, Lung, and Blood Institute (the ATS-DLD questionnaire)<sup>10</sup> and to return it to us in a stamped, self-addressed envelope. (A copy of the modified questionnaire is available on request from the authors.) Two weeks following the initial distribution of the questionnaires to the parents, another letter was sent as a reminder to parents who had failed to return a completed questionnaire.

In order to determine if nonrespondent parents and their children differed significantly in certain characteristics from those parents who had completed the questionnaires about their children, 200 nonrespondent parents were randomly selected and contacted by telephone by a trained research assistant four weeks after the questionnaires were initially sent to the parents. The parents were each read the part of the questionnaire that related most directly to cigarette smoking and respiratory illness. To ensure that the questions were answered accurately, these pertinent questions from the questionnaire were read aloud exactly as printed and without any elaboration by the research assistant.

### Pulmonary Function Measurements

Pulmonary function measurements were obtained from 89 chil-

\*From the Divisions of Ambulatory and Community Pediatrics and Pediatric Allergy and Pulmonary Disease, Department of Pediatrics, and the Department of Preventive and Environmental Medicine, The University of Iowa Medical School, Iowa City. This work was supported in part by Grant No. RR59 from the Clinical Research Center, by NIH Grant RR01 A10651-01, by Cystic Fibrosis Foundation Grant C 521 A, and by the Johnson County (IA) Lung Association.  
Manuscript received December 6, 1982; revision accepted June 29,

dren (47 girls and 41 boys) whose parents did not smoke and 94 children (52 girls and 42 boys) whose parents smoked. These children were randomly selected using tables of random numbers from the children for whom complete information was obtained using the questionnaire. All parents were requested to indicate their consent for pulmonary function studies to be obtained from their children, after we had provided a full written explanation of the reasons for obtaining the measurements and the procedures the child would follow during pulmonary function testing. Consent was obtained from 411 (85.6 percent) of the 484 children whose parents did not smoke and 596 (91.1 percent) of the 654 children whose parents smoked. When parental smoking was kept constant, the proportions of children who had cough with cold, cough apart from colds, or phlegm with or apart from colds were not significantly different for consenting parents compared to nonconsenting parents. We therefore felt that our sampling procedure produced a representative population of children.

Children were excluded if there was a history of recurrent respiratory illness or if there was any history of upper or lower respiratory infection during the prior six months. Spirometry was measured with a Jones Pulmonary waterless respirometer. Calculations of the parameters measured were done by the Jones Datamatic Computer with daily calibration. Lung volumes were measured by use of a plethysmograph (model 2000B, Cardiopulmonary Instruments) using a 3 L/second Fleisch temperature-controlled pneumotach, with a flow accuracy of  $\pm 1$  percent of full scale.

Each child was instructed in the measurement maneuver and was in an upright sitting position. Each test was repeated three to five times, and the best effort was taken. Flow rates and lung volumes were measured before and five minutes subsequent to 1.25 mg inhaled isoproterenol diluted with 2 ml normal saline solution and administered by an open nebulizer.

#### Analysis of Data

Discrete multivariate analysis was used to study the interactions among factors.<sup>22</sup> In this analysis, maternal and paternal smoking and gas cooking were treated as independent factors, while the frequencies of various respiratory symptoms or illness were the dependent variables. The reported prevalence of respiratory symptoms or illnesses were stratified by parental smoking (mother alone, father alone, both parents, either or both parents, neither parent smokes) and by cooking fuel use. Odds ratio was calculated for each interaction effect. Odds ratios greater than one indicated that the variable had a higher risk for the children and conversely, odds ratios of less than one indicated lower risk. A chi-square analysis was used to examine the significance of the odds ratio.

Regression lines were fitted to each of the pulmonary function measurements using the Statistical Analysis System (SAS) using the stepwise procedure.<sup>23</sup> The variables entered in the equation were

age in years, sex, weight (kg), and standing height (cm). Lines were fitted separately for children from smoking and nonsmoking environments, as well as for values obtained by pooling these two groups. F-tests were performed as described by Neter and Wasserman<sup>24</sup> to compare the fit of the lines obtained for values for children from the two environments and for the pooled data. Paired t-tests were used to compare the prebronchodilator and postbronchodilator pulmonary functions.

#### RESULTS

Completed questionnaires were obtained for 1,355 children, or 65.7 percent of the children six to 12 years of age in the school district. Of the 1,355 completed questionnaires, data on parental smoking history was complete for 1,138 (84 percent) of the children. In the remaining 217 questionnaires, either maternal or paternal or both smoking histories were unrecorded or incompletely recorded. The proportion of children with incomplete or no parental smoking history who had cough with or apart from colds, congestion or bringing up phlegm, or had chronic lung diseases was not statistically significantly different from the proportion of children with parental smoking histories who had these symptoms. These questionnaires were eliminated in subsequent analysis. Forty-nine percent of these children were males, and 51 percent were females. Five percent of the children had established diagnoses of chronic respiratory diseases. Two had cystic fibrosis, one had pulmonary tuberculosis, two had diagnoses of chronic bronchitis, and 49 had asthma. When we compared the 200 randomly selected nonrespondent families to our study population, we found no statistically significant differences in the proportion of parents who smoked at home. The proportions of children who had cough with colds, cough apart from colds, or who had congestion or bringing up phlegm with or apart from colds were not significantly different among the two groups.

Fifteen percent of the parents completing the questionnaire indicated they had bronchitis, emphysema, asthma, or other chronic respiratory condition. We found no relationship between the report of chronic respiratory illnesses in parents and the reported prevalence in children of symptoms of cough with colds,

Table 1—Proportion of Children with Cough with Colds or Hospitalized for Chest Problems Before Age 2 Years, by History of Parental Smoking and Home Cooking Fuel Used

Home Cooking Fuel	Parental Smoking History (Yes = Parent Smokes)		Percentage of Children Affected (Total Number of Children in the Group)	
	Father	Mother	Cough With Colds	Hospitalization For Chest Illnesses
Gas	No	No	32.8 (137)	5.1 (138)
Gas	No	Yes	33.7 (28)	7.1 (25)
Gas	Yes	No	35.6 (101)	8.0 (100)
Gas	Yes	Yes	30.6 (111)	9.8 (112)
Electricity	No	No	28.9 (34)	2.1 (24)
Electricity	No	Yes	37.7 (69)	8.8 (68)
Electricity	Yes	No	37.7 (69)	5.6 (178)
Electricity	Yes	Yes	44.5 (17)	11.2 (172)

Table 2—Association of Parental Smoking and Gas Cooking with Hospitalization of Children Before Age 2 Years for Respiratory Illnesses

Independent Variables	No. of Children Hospitalized for Chest Illnesses		Odds Ratio	SE	p-Value
	Yes	No			
Fuel used for home cooking					
Gas	28	350	2.4	0.694	0.001
Electricity	25	736	1.0	...	...
Parental smoking					
Father alone smokes	18	260	2.3	0.856	0.022
Mother alone smokes	8	90	2.9	1.279	0.026
Father and mother smoke	13	271	1.6	0.856	0.21
Either or both parents smoke	39	621	2.1	0.666	0.017
Neither parent smokes	14	465	1.0	...	...

enough apart from cold, or bringing of phlegm with or apart from colds. Of the 1,138 children, 31 percent lived in homes where gas was used for cooking, and 69 percent lived in homes where electricity was used for cooking. There was a significant association between parental smoking and the use of gas for cooking. Fathers smoked in 224 (56.4 percent) of the 397 homes where gas was used for cooking, compared to 366 (46.6 percent) of the 786 homes in which electricity was used for cooking ( $\chi^2 = 10.28$ ,  $p < 0.001$ ). Similarly, mothers smoked in 180 (40.8 percent) of the 441 homes in which gas was used for cooking, compared to 292 (33.7 percent) of the 866 homes in which electricity was used for cooking ( $\chi^2 = 6.33$ ,  $p < 0.05$ ). The proportion of children with chronic respiratory symptoms by parental smoking and use of cooking fuel are shown in Table 1.

The use of gas for cooking was associated with an increased risk of hospitalization of the children before age two years because of chest colds and other respiratory illnesses (odds ratio = 2.4) independent of parental smoking (Table 2). Any parental smoking also increased the odds ratio. When both parents smoked in a household in which gas was used for cooking, the odds ratio was 9.25 ( $p = 0.0006$ ). The use of gas for cooking was not associated with increased risk of occurrence of cough with colds in the children. How-

ever, parental smoking increased the risk of occurrence of these symptoms (Table 3). Other than the possibility of wheezing and whistling sounds in the chest with colds, none of the dependent variables in Table 4 was significantly associated with parental smoking and/or use of gas for cooking. Also, the frequency of occurrence of ear infections in the children between ages 0 to two years, or two to five years, or the occurrence of wheezing with exercise was not found to be associated with parental smoking or use of gas for cooking.

The mean standing height of 144.2 cm and weight of 37.8 kg for children whose parents smoked was not significantly different from the mean standing height of 145.6 cm and weight of 38.7 kg for children whose parents did not smoke. Mean values for initial measurements of pulmonary function before the inhaled isoproterenol did not differ significantly between children from smoking and non-smoking families. Significant differences in mean values were not seen after bronchodilator inhalation in the children from non-smoking families, but were apparent among children from smoking families for the measurements of FEF75, FEV<sub>1</sub>, and FEF25-75 (Table 5). The mean values of the measurements of lung volumes for the two groups of children were not statistically different. Because 28 *t*-tests were performed for these analyses, adjustment was made by accepting only *t*-tests with *p*

Table 3—Association of Parental Smoking and Gas Cooking with Occurrence of Cough with Colds in Children

Independent Variables	No. of Children with Symptoms of Coughs with Colds		Odds Ratio	SE	p-Value
	Yes	No			
Fuel used for home cooking					
Gas	125	252	0.9	0.123	0.55
Electricity	266	495	1.0	...	...
Parental smoking					
Father alone smokes	100	177	1.4	0.228	0.023
Mother alone smokes	36	61	1.5	0.348	0.084
Father and mother smoke	111	173	1.6	0.255	0.012
Either or both parents smoke	247	411	1.5	0.194	0.001
Neither parent smokes	144	366	1.0	...	...



Table 4—Relationship of Parental Smoking and Cooking Gas with Occurrence of Respiratory Symptoms in Children

Independent Variable	No. of Children with Respiratory Symptoms		Odds Ratio	SE	p-Value
	Yes	No			
1. Chest congestion and phlegm with colds					
Gas	70	307	1.1	0.188	0.41
Electricity	136	633	1.0	...	...
Father alone smokes	46	230	1.0	0.213	0.82
Mother alone smokes	19	78	1.3	0.363	0.40
Father and mother smoke	84	229	1.2	0.383	0.28
Either or both parents smoke	119	307	1.2	0.186	0.35
Neither parent smokes	77	403	1.0	...	...
2. Chest congestion and phlegm apart from cold					
Gas	17	345	1.0	0.302	0.99
Electricity	35	708	1.0	...	...
Father alone smokes	12	258	0.9	0.345	0.86
Mother alone smokes	7	87	1.6	0.730	0.30
Father and mother smoke	11	264	0.8	0.317	0.64
Either or both parents smoke	30	609	1.0	0.286	0.98
Neither parent smokes	22	444	1.0	...	...
3. Wheezing and whistling sounds in chests with colds					
Gas	104	273	1.0	0.154	0.56
Electricity	198	564	1.0	...	...
Father alone smokes	74	202	1.2	0.210	0.27
Mother alone smokes	30	67	1.5	0.362	0.12
Father and mother smoke	86	198	1.4	0.241	0.03
Either or both parents smoke	190	467	1.3	0.165	0.03
Neither parent smokes	112	370	1.0	...	...
4. Wheezing and whistling sound in chest apart from colds					
Gas	29	326	0.9	0.222	0.80
Electricity	61	647	0.1	...	...
Father alone smokes	24	235	1.2	0.329	0.52
Mother alone smokes	14	73	2.2	0.761	0.02
Father and mother smoke	16	244	0.6	0.239	0.39
Either or both parents smoke	54	552	1.1	0.257	0.55
Neither parent smokes	36	421	1.0	...	...
5. Attacks of wheezing with shortness of breath					
Gas	30	346	0.7	0.158	0.12
Electricity	83	679	1.0	...	...
Father alone smokes	26	251	0.8	0.211	0.48
Mother alone smokes	12	85	1.1	0.389	0.70
Father and mother smoke	22	261	0.7	0.191	0.14
Either or both parents smoke	60	897	0.8	0.161	0.29
Neither parent smokes	53	429	1.0	...	...

values of  $<0.002$  as significantly different at a 0.05 confidence level ( $0.05 + 28 = 0.002$ ). The mean percentage changes in the pulmonary function measurements (calculated as the differences between the postvalue and prevalue divided by the prevalues for each patient), however, did not differ significantly between the two groups of children (using an unpaired *t*-test).

#### Discussion

Respiratory symptoms and illnesses occur fre-

quently, particularly in the temperate regions of the worlds in preschool and school-age children. Only recently has it been appreciated that parental smoking at home may be associated with an increased risk of occurrence of respiratory symptoms in children. A higher rate of hospitalization of the children before age two years for chest illnesses (bronchitis, pneumonia, etc) was associated with both parental smoking and gas cooking. A significant increase in pulmonary function after an inhaled bronchodilator among children of

2023379674

Table 5—Flow Rates of Children Before and After Inhaled Isoproterenol

Variables	Children of Smoking Parents			Children of Nonsmoking Parents		
	Mean (SE) Measurements of Flow Rates and Lung Volumes			Mean (SE) Measurements of Flow Rates and Lung Volumes		
	Preisoproterenol	Postisoproterenol	p*	Preisoproterenol	Postisoproterenol	p*
PEFR	8.11 (0.13)	4.97 (0.13)	0.11	5.10 (0.13)	5.05 (0.12)	0.42
FEF25	4.18 (0.12)	4.15 (0.12)	0.71	4.34 (0.11)	4.21 (0.11)	0.11
FEF50	3.22 (0.09)	3.35 (0.09)	0.02	3.25 (0.09)	3.36 (0.09)	0.07
FEF75	1.52 (0.05)	1.76 (0.07)	0.0001†	1.56 (0.06)	1.69 (0.07)	0.11
FEV <sub>1</sub>	2.23 (0.05)	2.27 (0.05)	0.0002†	2.21 (0.05)	2.23 (0.06)	0.34
FEV <sub>1</sub>	2.52 (0.06)	2.52 (0.06)	0.48	2.47 (0.06)	2.50 (0.07)	0.17
FEF25-75	2.60 (0.08)	2.82 (0.08)	0.0001†	2.60 (0.07)	2.78 (0.09)	0.03
FVC	2.55 (0.06)	2.57 (0.06)	0.18	2.51 (0.07)	2.53 (0.07)	0.13

\*Paired t-test comparing initial pulmonary function measurements and postbronchodilator values.

†Significant at 0.05 level after adjusting for the performance of 26 t-tests.

smoking parents is an interesting additional observation perhaps consistent with previous reports of increased bronchial reactivity in cigarette smokers with normal lung function<sup>20</sup> and an association between symptomatic asthma in children and parental smoking.<sup>21</sup>

Parental smoking may be associated with different types of respiratory illnesses in infancy compared to the school age. Fergusson et al<sup>22</sup> found an increased risk of infantile lower respiratory illnesses in the last eight months of the first year of the infant's life to be associated with maternal but not paternal smoking. Similarly, Colley et al<sup>23</sup> found that infantile pneumonia was more common when both parents smoked than when neither parent smoked. The risk was intermediate when only one parent smoked. These results are consistent with our findings that hospitalization of children in the first two years of life for bronchitis and pneumonia was associated with parental smoking. However, Fergusson et al<sup>22</sup> did not study the association of parental smoking and use of gas for cooking on respiratory infection rates. Their study is different from ours also, in that they studied respiratory infection rate between four and 12 months of life. Their study was prospective-retrospective in design, and therefore, parental recall may have been more reliable than in our study. In the first year of life, an infant is likely to spend proportionately more time with the mother than the father. Thus, the age of the child at the time of the administration of the respiratory questionnaire may have been an important factor in the finding that maternal but not paternal smoking was associated with respiratory illness in the child.

Weiss et al<sup>24</sup> reported a dose response between prevalence rate of symptoms of persistent wheezing, cough, and phlegm in children and parental smoking. The rate of occurrence of symptoms in children was highest when both parents smoked, intermediate when either parent smoked, and lowest when no

parent smoked. However, the authors also found a strong association between the occurrence rate of these symptoms in the children and the prevalence rate for such symptoms in the parents. We found a significant association between parental smoking and the prevalence of cough with colds in the children. However, we did not find any association between parental smoking or the use of gas cooking and the reported incidence of cough apart from colds and chest congestion and bringing up phlegm with or apart from colds. In a study of children whose ages were similar to the children in our population, however, Colley<sup>23</sup> found an association between parental smoking and the occurrence of cough during the day or at night in winter in the children. He also found an association between parental smoking and bringing up "any phlegm from the chest first thing in the morning in winter" by the children. The lack of association between these variables and parental smoking in our study may be attributable to the phrasing of the questions in the ATS-DLD questionnaire, where "in the morning" was not specifically mentioned, and where phlegm production was sought in association with chest colds rather than "in winter." Slight changes in the phrasing of questions can result in substantial differences in the type of responses one obtains.<sup>25,26</sup>

Flory et al<sup>27</sup> showed an association between the levels of NO<sub>2</sub> in kitchens and bedrooms of the homes and the prevalence of respiratory illness in primary school-children. This association was independent of the children's age, sex, social class, and the number of cigarettes smoked at home. In another study, children six to 11 years old from households with gas stoves had a history of more frequent respiratory illnesses before age two years compared to children from homes where gas was not used for cooking.<sup>28</sup> In a study of schoolchildren in England and Scotland, a reported incidence of coughs, colds going to the chest, and bronchitis in children from homes using gas for cooking

was significantly higher than for children from homes where electricity was used.<sup>22</sup> Melia et al<sup>23</sup> demonstrated that the association between respiratory illness and gas cooking tended to disappear as the children grew older.

The nature of the association of respiratory symptoms in children and gas cooking in the home is yet unclear. Two oxides of nitrogen, nitric oxide (NO) and nitrogen dioxide (NO<sub>2</sub>), are produced in varying concentrations in homes with gas stoves.<sup>24-26</sup> It has been observed that acute exposure of man and animals to high levels of nitrogen dioxide (NO<sub>2</sub>) can cause pulmonary edema and death.<sup>27</sup>

A significant reduction in FEF<sub>25-75</sub> values was observed in children who smoked, as well as in children whose parents smoked but who were non-smokers themselves.<sup>28</sup> At least one group of investigators has found no association between parental smoking and lung function measurements of the children.<sup>29</sup> In these studies, the children did not receive an inhaled bronchodilator drug. Inhaled bronchodilator medication was administered to children in our study, and we observed statistically significant differences in the mean values of FEF<sub>75</sub>, FEV<sub>1</sub>, and FEF<sub>25-75</sub> for children whose parents smoked compared to those whose parents did not smoke. The clinical importance of such observed differences in the absolute values of pulmonary function measurements is, however, unclear.

In a recent study of children six to 11 years old from households with gas stoves, small but significant differences were found in FEV<sub>1</sub> and FVC corrected for height, compared to children from homes where gas was not used for cooking.<sup>30</sup> These families tended to be poorer and were in the lower socioeconomic class. Flory et al<sup>31</sup> found no significant relationship between lung function measurements and concentrations of NO<sub>2</sub> in either kitchen or bedroom. Lung function measurements of peak expiratory flow rates (PEFR) and FEF<sub>25-75</sub> for children from homes with gas stoves were not significantly higher than measurements for children from homes with electric stoves. Hasselblad et al,<sup>32</sup> however, found pulmonary function suggestively decreased among nine- to 13-year-old girls in homes with gas stoves and not among younger children.

Based on the findings of this report and from previously published findings, one is led to conclude that parental smoking is associated with a risk of certain respiratory illnesses and symptoms among children living in the same environment. An independent but similar effect is suggested for gas cooking. Children from homes where parents smoke had increased reactivity of airways after bronchodilator therapy, but it is not known if these changes persist or have clinical consequences.

## REFERENCES

- Colley JRT, Holland WW, Corkhill RT. Influence of passive smoking and parental phlegm on pneumonia and bronchitis in early childhood. *Lancet* 1974; 2:1031-34.
- Harlap S, Davies AM. Infant admissions to hospital and maternal smoking. *Lancet* 1974; 1:529-32.
- Fergusson DM, Horwood LJ, Shannon FT. Parental smoking and respiratory illness in infancy. *Arch Dis Child* 1980; 55:354-61.
- Bland M, Bewley BR, Pollard V, Banks MH. Effect of children's and parents' smoking on respiratory symptoms. *Arch Dis Child* 1978; 53:100-105.
- Florey CV, Melia RJW, Chinn S, Goldstein BD, Brooks AGF, John HM, et al. The relationship between respiratory illness in primary schoolchildren and the use of gas for cooking. III. Nitrogen dioxide, respiratory illness and lung infection. *Int J Epidemiol* 1979; 8:347-53.
- Melia RJW, Florey CV, Chinn S. The relation between respiratory illness in primary schoolchildren and the use of gas for cooking. I. Results from a national survey. *Int J Epidemiol* 1979; 8:333-38.
- Colley JRT. Respiratory symptoms in children and parental smoking and phlegm production. *Br Med J* 1974; 2:201-04.
- Cameron P, Kistin JS, Zaks JM, Wolfe JH, Tighe G, Oslett B, et al. The health of smokers' and nonsmokers' children. *J Allergy* 1969; 43:336-41.
- Weiss ST, Tager IB, Speizer FE, Rosner H. Persistent wheeze: its relation to respiratory illness, cigarette smoking, and level of pulmonary function in a population sample of children. *Am Rev Respir Dis* 1980; 122:697-707.
- Cortinaker SL, Walker DK, Jacobs FH, Rick-Harris H. Parental smoking and the risk of childhood asthma. *Am J Public Health* 1982; 72:574-79.
- Tager IB, Weiss ST, Rosner H, Speizer FE. Effect of parental cigarette smoking on the pulmonary function of children. *Am J Epidemiol* 1979; 110:15-26.
- Hasselblad V, Humble CG, Graham MG, Anderson HS. Indoor environmental determinants of lung function in children. *Am Rev Respir Dis* 1981; 123:479-85.
- Speizer FE, Ferris B, Bishop YMM, Sprugler J. Respiratory disease rates and pulmonary function in children associated with NO<sub>2</sub> exposure. *Am Rev Respir Dis* 1980; 121:3-10.
- Ferris BG. Epidemiology standardization project. *Am Rev Respir Dis* 1978; 118:1-120.
- Bishop YMM, Fienberg S, Holland P. Discrete multivariate analysis. Cambridge: MIT Press, 1975.
- Dixon WJ. BMDP. Statistical software, 1981. Los Angeles: University of California Press, 1981.
- Barr AJ, Gooding JH, Sall JP. Stepwise procedures. In: Helwig JT, Council CA, eds. SAS user's guide, 1979 edition. Raleigh, NC: SAS Institute Inc, 1979:391-96.
- Neter J, Wasserman W. Applied linear statistical models. Homewood, IL: Richard D. Irwin, Inc, 1974:87-89.
- Gerrard JW, Cockerill DW, Mink JT, Cotton DJ, Punawala R, Dorman JA. Increased nonspecific bronchial reactivity in cigarette smokers with normal lung function. *Am Rev Respir Dis* 1980; 122:577-81.
- Cumstuck GW, Tuckman MS, Helwig KJ, Hennessy KM. Standardized respiratory questionnaires: comparison of the old with the new. *Am Rev Respir Dis* 1979; 119:45-53.
- Helwig KJ, Cumstuck GW, Speizer FE, Ferris BC, Lebowitz D, Tuckman MS, et al. Comparison of three standardized questionnaires on respiratory symptoms. *Am Rev Respir Dis* 1979; 120:1221-31.
- Melia RJW, Florey CV, Altman DG, Swan AV. Association between gas cooking and respiratory disease in children. *Br Med J* 1977; 2:149-52.

- 23 Melia RJW, Florey CV, Darby SC, Palmes ED, Goldstein BD. Differences in NO<sub>x</sub> levels in kitchens with gas or electric cookers. *Atmos Environ* 1978, 12:1379-81
- 24 Cole WA, Wade WA, Yocum JE. A study of indoor air quality. Washington, DC: US Government Printing Office 1974 (United States Environmental Protection Agency Publication No. EPA-650/4-74-042)
- 25 Goldstein BD, Melia RJW, Chinn S, Florey CV, Clark D, John HH. The relation between respiratory illness in primary schoolchildren and the use of gas for cooking II. Factors affecting nitrogen dioxide levels in the home. *Int J Epidemiol* 1979, 8:339-45
- 26 US Environmental Protection Agency. Scientific and Technical Data Base for Criteria and Hazardous Pollutants, 1975. ERC/RTII Review EPA Publications No. EPA-600/1-76-023, 191-229
- 27 Schilling RSF, Letai AD, Hui SL, Beck GL, Schoenberg JB, Bouhuys A. Lung function, respiratory disease, and smoking in families. *Am J Epidemiol* 1977, 106:274-83

### Myocardial Protection via the Coronary Sinus

The First International Symposium on Myocardial Protection via the Coronary Sinus will be held at the Hotel InterContinental Vienna, Vienna, Austria, February 27-29, 1984. For information, contact the Secretariat, c/o Interconvention, PO Box 80, A-1107 Vienna, Austria.

### Diagnostic Imaging

The Department of Radiology, Duke University Medical Center, will present this five-day postgraduate course at the Hyatt Regency Cancun Hotel, Cancun, Mexico, February 12-17, 1984. For information, contact Donald R. Kirks, M.D., Department of Radiology, Duke University Medical Center, Box 3834, Durham, North Carolina 27710 (919.681-2711, ext 286 or 287).

2023379677

2023379678

Lebowitz, M.D., Knudson, R.J., Burrows, B. "Family Aggregation of Pulmonary Function Measurements" Am Rev Respir Dis 120: 8-11, 1984.

SUMMARY: Family aggregation of pulmonary function measurements was analyzed in the nuclear families of the Tucson epidemiologic study of airway obstructive diseases (AOD). There were 271 parental pairs and their natural children who had satisfactory pulmonary function data. Initial regression analysis showed significant correlations of the pulmonary function variables after controlling for age and sex. Body habitus, as measured by the Ponderal Index, was highly aggregated as well. Pulmonary function measurements were aggregated in families independent of family size, reported diagnosed AOD, and children's smoking, even though both asthma and smoking showed significant familial aggregation. After controlling for the familial aggregation of body habitus, a major determinant of pulmonary function, there was no remaining independent aggregation of pulmonary function measurements. It was also determined that parental passive smoking had no effect on children's pulmonary function measurements.

2023379679

# Family Aggregation of Pulmonary Function Measurements<sup>1-3</sup>

MICHAEL D. LEBOWITZ, R. J. KNUDSON, and B. BURROWS

## Introduction

Clinicians have noted that airways obstructive diseases, especially emphysema, appear to run in families, and this has been a common observation since the early nineteenth century (1, 2). Except for the rare homozygotic alpha<sub>1</sub>-antitrypsin deficiency, other genetic predispositions to chronic obstructive diseases have not been clearly demonstrated (3). Studies in England have demonstrated that there is a genetic basis of asthma (4, 5). Recent studies have demonstrated aggregation of pulmonary function in twins (6, 7), and recent population studies have shown that pulmonary function measurements appear to be aggregated in families (8-10).

It has long been recognized that body size and configuration are genetically determined, yielding familial aggregation of body habitus; body habitus has a major influence on pulmonary function. Although adjustment for height to predict a person's lung function is standard, this is not sufficient when examining interindividual correlations of body habitus with lung function. Thus, it is necessary to evaluate the interaction of body habitus in the analysis of familial aggregation of pulmonary function.

This report attempts to examine the relationship of pulmonary function measurements in the family, of body habitus relationships in the family, and the interaction thereof. The influence of a history of airways obstructive disease in parents and children, smoking in parents and children, family size, and the influence of passive smoking, which are possible confounding variables, are examined as well.

## Methods

Data on nuclear families reported herein are derived from the Tucson Epidemiological Studies of Airways Obstructive Diseases, which has been described previously (11). The population under study is a multistage stratified cluster sample of white, non-Mexican-American families in the Tucson area,

**SUMMARY** Family aggregation of pulmonary function measurements was analyzed in the nuclear families of the Tucson epidemiologic study of airway obstructive diseases (AOD). There were 271 parental pairs and their natural children who had satisfactory pulmonary function data. Initial regression analysis showed significant correlations of the pulmonary function variables after controlling for age and sex. Body habitus, as measured by the Ponderal index, was highly aggregated as well. Pulmonary function measurements were aggregated in families independent of family size, reported diagnosed AOD, and children's smoking, even though both asthma and smoking showed significant familial aggregation. After controlling for the familial aggregation of body habitus, a major determinant of pulmonary function, there was no remaining independent aggregation of pulmonary function measurements. It was also determined that parental passive smoking had no effect on children's pulmonary function measurements.

AM REV RESPIR DIS 1984; 129:1-11

where stratification was on age of head of household and on socioeconomic status.

In the first year of this study (1972-1973), questionnaires were completed on all subjects. These included a respiratory history and a family history with a family tree. Subjects 12 yr of age and older completed their own questionnaires. Mothers, or substitutes if the mothers were not available, completed them for children younger than 12 yr of age (11). Comparisons of maternal and self reporting performed for smoking histories showed no discrepancies. A separate study showed no significant differences, in children 8 to 11, in parental versus self reporting of chronic symptoms (12). Pulmonary function tests were performed satisfactorily in over 90% of those 6 yr of age and older, using techniques previously described (13).

Nuclear families were defined as families in which there were a mother, a father, and at least one natural child of the pair. There were 344 nuclear families of the 1,655 families studied (approximately 25%). The number of subjects involved in these nuclear families represent about 1,400 of the 3,800 subjects in the total study population. There were 271 families in which both parents and 1 or more of their children had satisfactory pulmonary function measurements in the first year of the study. These were analyzed as units. We also considered relationships between parent-child pairs, spouse pairs, and sibling pairs.

The presence of airway obstructive disease in the children and the parent was obtained from the questionnaires, as was smoking history (for those 15 yr of age and older). Family size, obtained from household records, was also used to determine if it was a confounding variable.

As previously described, all measurements were made by trained nurse inter-

viewers; tests of interobserver variability in all measurements indicated no significant differences (11, 13). Standing height (H) in inches, sitting height in inches, and weight (W) in pounds were used to calculate the Ponderal Index (14), an index of body habitus (i.e.,  $H/\sqrt{W}$ ). This index had the best correlation with pulmonary function measures when compared with other indexes of body habitus.

The pulmonary function measurements used were: forced vital capacity (FVC), forced expiratory volume in one second (FEV<sub>1</sub>), and maximal expiratory flows at 50 and 75% of the FVC had been expired ( $\dot{V}_{max_{50}}$  and  $\dot{V}_{max_{75}}$ , respectively). Each subject's function was first corrected for height and weight, using regression equations derived from data on asymptomatic nonsmokers in this population. These corrected values did not explain all effects of body habitus.

Comparisons of children's and parents' pulmonary function variables (expressed percent predicted) were performed first before accounting for parental body habitus; these were performed before and after Z-score transformations. The Z-scores are standard normal variates; for each subject the observed value was subtracted from

(Received in original form October 13, 1982; in revised form May 2, 1983)

<sup>1</sup> From the Division of Respiratory Sciences (Westend Research Laboratories), The University of Arizona College of Medicine, Tucson, Arizona.

<sup>2</sup> Supported by SCOR Grant No. HL-14 from the National Heart, Lung and Blood Institute.

<sup>3</sup> Requests for reprints should be addressed to Michael D. Lebowitz, Ph.D., The University of Arizona Health Sciences Center, Division of Respiratory Sciences, Tucson, AZ 85724.

2023379680

group mean and divided by the group standard deviation ( $Z_i = (X_{ijk} - \bar{X}_{jk})/s_{jk}$ , for each  $i$  subject,  $j$  age group,  $k$  sex). This removed further effects of age and sex and gave all values the same units. All pulmonary function variables were then adjusted for the individual child's Ponderal Index and the parental Ponderal Indexes (where significantly correlated with the pulmonary function variables) using regression techniques. The Z-scores were recalculated for each of these pulmonary function variables within each age-sex group represented in the parent-child pairs. The Z-score technique is useful for looking at specific effects of other explanatory variables, such as smoking.

Familial aggregation was estimated by analysis of variance (ANOVA), which corresponds to the intraclass correlation as described by Donner and Koval (15). These investigators demonstrated that this method was slightly better than the maximal likelihood estimator if the true correlation was likely to be less than 0.5. Both were better than the usual product-moment correlation method. They also demonstrated that differences in results with inclusion or exclusion of one child were minimal and nonsignificant. The multivariate components of variance method of ANOVA is more useful than other methods of examining aggregation in that it gives separate estimators for variance components and allows usual testing of significance of those estimates. Analyses of variance were performed using the children's pulmonary function measurements as the dependent variable, using age, sex, smoking, and body habitus indexes of the children and the parents as covariates, with parents' pulmonary function (as continuous variables) as the explanatory variables (main effects) in the ANOVA. Covariates were all continuous variables except sex. Main effects were grouped into equal thirds. Two- and three-way interactions were examined. The regression option was used to remove covariate effects, other main effects, and interaction effects from the contribution of each main factor, using SPSS programs on a DEC-10 Cyber 175 University Computer System. In the case of nuclear family analyses using analyses of variance, the analyses were done for all families and separately and for those with 2 or more children (13). For analysis of parent-child pairs, the male/female oldest child was used. For analysis of sibling pairs, the 2 oldest children of each sex in the family were used.

### Results

The characteristics of members of the nuclear families with pulmonary function tests are shown in table 1. There were highly significant product-moment correlations of measures of body habitus between all children and their parents, after adjusting for age and sex.

TABLE 1  
CHARACTERISTICS OF PARENTS AND CHILDREN  
(6 YEARS OF AGE AND OLDER) IN NUCLEAR  
FAMILIES WITH PULMONARY FUNCTION

Characteristics	Children (n = 354)		Mothers (n = 278)		Fathers (n = 268)	
	Mean	SD	Mean	SD	Mean	SD
Age	13.5	6.0	36.1	6.8	36.4	12.2
Height (H) (in.)	60.8	7.5	63.9	2.3	68.3	2.5
Weight (W) (lb.)	108.4	41.0	134.8	24.8	172.5	24.8
H/W <sup>1/3</sup>	13.1	0.8	12.5	0.7	12.5	0.5
%FVC	110.3	23.9	102.3	16.5	101.2	15.0
%FEV <sub>1</sub>	108.5	21.3	104.8	18.9	104.2	17.5
Ever smokers, %	1.7*		80.0		72.3	

Definition of abbreviations: %FVC = percent predicted forced vital capacity; %FEV<sub>1</sub> = percent predicted forced expiratory volume in one second.

\* n = 181, 15 yr of age and older only.

The linear regression of all the children's H/W<sup>1/3</sup> on mothers' H/W<sup>1/3</sup> had a correlation ( $r$ ) of 0.804 ( $p < 0.0001$ ); with fathers,  $r$  was 0.773 ( $p < 0.0001$ ). There were also some significant product-moment correlations of the amount of smoking (pack-years) between various pairs, especially between fathers and children siblings and spouses ( $p < 0.001$ ), even though many fewer children than parents smoke. The significant correlations were between father and both daughters and sons, between siblings, and between spouses; the mothers-sons correlation of smoking was borderline ( $p = 0.085$ ). There was no correlation of smoking with any of the measurements of body size or habitus.

Product-moment correlations between children's and parents' pulmonary function measurements were statistically significant ( $r$  as much as 0.30) prior to adjusting for covariates. The most significant aggregation of a pulmonary function measurement prior to body habitus correction was with FVC, which as a volume measurement is most closely correlated with body habitus. The relationships were also strong and significant for FEV<sub>1</sub>, but were less often significant for the flow variables.

However, regressions of the children's percent predicted pulmonary function against parents' pulmonary function and body habitus measurements showed significant correlations of the children's pulmonary function with the parents' body habitus, as well as with their own body habitus. After body habitus and age corrections, the previous correlations of pulmonary function variables between any of the pairs were no longer present. Thus, the relation between children's lung function and parents' lung function is likely to be related to their similar body habitus.

Despite the aggregation of asthma (table 2), it was not a factor in the aggregation of pulmonary function measurements when tested by ANOVA. There was no family aggregation of present diagnosed chronic bronchitis for emphysema. The presence of these other airway obstructive diseases in parents and/or children were not factors in the relationships between pulmonary function measurements in the family (by ANOVA). Family size was not found to be a significant factor in any of the analyses. Analyses of variance for families with 2 or more children only, as well as for all families (1 child or more), yielded similar results.

TABLE 2  
PHYSICIAN-CONFIRMED EVER ASTHMA IN NUCLEAR FAMILIES

	No Asthma in Parents	One Parent with Asthma	Both Parents With Asthma
Families, n	273	68	3
Families with 1+ asthmatic child, %	10.8*	28.5	100
Oldest children with asthma, %	8.8	19.1	33.3
Children, n	838	122	11
Children with asthma, %	6.5*	19.7	63.6

\* Rates of asthma significantly higher with one or more asthmatic parents ( $p < 0.005$ ).

2023379681



TABLE 3

CHILDREN'S VOLUME AND FLOW MEASUREMENTS IN RELATION TO PARENTS' VOLUME AND FLOW MEASUREMENTS, CONTROLLING FOR OTHER VARIABLES (BY ANOVA)\*

	df	FVC			$\dot{V}_{max_{25}}$		
		Mean Square	F	p	Mean Square	F	p
No controls							
Father's function	2	3,086.1	8.87	0.001	1,837.5	2.57	0.078
Mother's function	2	2,248.4	4.84	0.008	1,551.8	2.44	0.086
Interaction	4	319.9	0.89	0.600	417.1	0.66	0.624
Explained	8	1,756.2	3.78	0.001	977.4	1.54	0.145
Age, sex, and smoking controls							
Covariate†	6	4,185.3	10.89	0.001	2,742.5	4.88	0.001
Father's function	2	919.8	2.39	0.084	1,031.3	1.78	0.174
Mother's function	2	1,369.2	3.55	0.030	1,475.8	2.52	0.083
Father's smoking	2	388.8	0.70	0.499	1,386.5	2.33	0.099
Mother's smoking	2	42.8	0.11	0.895	1,128.8	1.93	0.148
2-way interactions‡	24	482.3	1.25	0.198	863.1	0.98	0.519
Explained	37	1,278.2	3.31	0.001	1,052.1	1.80	0.005
Age, sex, and habitus controls,‡ adjusted children's function†							
Covariate†	4	1,482.8	8.72	0.001	1,831.8	3.55	0.040
Father's function	2	511.4	2.00	0.138	408.1	0.84	0.529
Mother's function	2	374.9	1.08	0.343	88.1	0.14	0.674
2-way interactions	24	487.9	1.91	0.009	944.9	1.48	0.078
3-way interactions	32	382.1	1.49	0.052	420.4	0.86	0.921
Explained	68	623.4	2.44	0.001	770.5	1.21	0.163

Definition of abbreviations: df = degrees of freedom; FVC = forced vital capacity;  $\dot{V}_{max_{25}}$  = maximal flow after exhalation of 80% of FVC; F = variance ratio.

\* "Regression option" (see text).

† Total = 257 without habitus controls, less with habitus data, as complete data missing from 1 or more members of some families.

‡ Parents' habitus also as main effects.

§ No three-way interactions.

|| Children's function adjusted for their and parents' body habitus (using the Ponderal Index).

¶ All ages, children's sex and smoking/habitus.

To account for all of the possible significant covariables and interactions, we used multivariate analysis of variance to evaluate aggregation of FVC, FEV<sub>1</sub>,  $\dot{V}_{max_{25}}$ ,  $\dot{V}_{max_{50}}$ . Each explanatory variable was treated as an independent contributor to the dependent variable. The results for all 4 pulmonary function variables were similar, so only 1 volume (FVC) and 1 flow ( $\dot{V}_{max_{25}}$ ) variable are shown (table 3).

Without covariate controls or adjusted children's pulmonary function, the parents' volume measurements contributed significantly to the explanation of the children's measurements. These significant relationships for FVC, FEV<sub>1</sub>, and  $\dot{V}_{max_{25}}$  were also present after age and sex were used as covariates and parental smoking was used as explanatory variables (table 3). However, adjusting for smoking reduced the significance of fathers' FVC and both parents'  $\dot{V}_{max_{25}}$ . Parents' smoking was significant only for  $\dot{V}_{max_{25}}$  (maternal smoking only). Furthermore, we did not find any relation between fathers' or mothers' smoking and their spouses' pulmonary function.

The body habitus-corrected FVC and

$\dot{V}_{max_{25}}$  of the children as the dependent variables had no significant relationship with any of the explanatory variables, where both the parents' pulmonary function variables had been corrected for body habitus as well. The total amount of variability explained in these analyses was significant for FVC and FEV<sub>1</sub> ( $p = 0.001$ ).

The analyses of variance performed on the pulmonary function measurements of parent-oldest child, spouse, or sibling pairs yielded negative results.

There were two exceptions to this: the contribution of the father's  $\dot{V}_{max_{25}}$  on the daughter's  $\dot{V}_{max_{25}}$  was significant ( $p = 0.046$ ); however, the total variance explained was not significant. As that only left 1 of 24 comparisons significant, mother-son FVC ( $p$  of main effect = 0.028), and one might expect approximately 1 of these many comparisons ( $n = 24$ ) to be significant by chance alone (at  $p < 0.05$ ), this was considered a chance finding. Performing the same analyses after correcting for smoking habits in the parents and children, and after analyzing by whether airways obstructive diseases were present or not, did not change the results.

The children's Z-score-corrected pulmonary function variables were compared among smoking and nonsmoking parents; the results are shown in table 4. As can be seen, parental smoking did not have a significant effect on children's pulmonary function; smoking habits of others in the household (predominantly siblings) did not have any effect either.

### Discussion

It is generally agreed that body habitus is genetically determined; it certainly has high familial aggregation. Pulmonary function variables are measurements that are highly dependent on various characteristics of body habitus. Pulmonary function measurements have previously been shown to aggregate in families when body habitus in the families was not accounted for (8, 9). In our study, we first saw strong correlations between parents' and children's pulmonary function measurements, significant for FVC, FEV<sub>1</sub>, and  $\dot{V}_{max_{25}}$ . However, when we controlled for body habitus in the examination of the relationship between parents' and

TABLE 4

Z VALUES OF CHILDREN'S PULMONARY FUNCTION BY PARENTAL SMOKING

Parental Smoking	n	FVC		FEV <sub>1</sub>		$\dot{V}_{max_{25}}$		$\dot{V}_{max_{50}}$	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
Neither	48	-0.08	1.00	-0.12	0.99	-0.16	1.19	-0.08	1.08
Mother smokes	36	-0.16	0.83	-0.16	0.81	-0.15	0.85	0.0	0.88
Father smokes	82	-0.08	0.91	-0.04	0.87	-0.17	0.95	-0.17	1.01
Both smoke	98	+0.19	1.08	+0.23	1.06	+0.15	0.99	+0.20	0.97
Total	271	0.01	0.89	0.03	1.00	0.0	1.00	0.0	1.00
df		Mean Square		Mean Square		Mean Square		Mean Square	
Between	3	1.578		2.212		1.386		2.314	
Within	267	0.987		0.979		0.992		0.982	
F		1.632		2.269		1.396		2.358	
p		0.182		0.081		0.244		0.072	

For definition of abbreviations, see table 3.

children's pulmonary function measurements, we no longer found such relationships. Thus, familial correlations for observed pulmonary function, especially FVC, were dependent on familial aggregation of body habitus, even after controlling for age and sex. It can not be construed as an overadjustment of familial data, as the underlying, familial aggregation is one of body habitus characteristics. This is more a genetic effect than one of dietary or environmental effect, as shown by the weaker relationship between siblings and the lack of a relationship of body habitus between spouses.

On the other hand, we did detect a familial relationship of asthma between children and parents independent of smoking and pulmonary function measures (table 2), which confirmed findings of Sibbald and coworkers (4, 5), and Townley and associates (16). To insure that this is not strictly a result of reporting bias, objective measures such as bronchial-reactivity would have to be done to confirm the relationship, as has been done by Townley and associates (16). This familial aggregation of asthma did not affect the findings for any familial aggregation of pulmonary function.

We found also that smoking habitus aggregated in families but was probably an environmental influence only. Spouses and siblings had the closest relationships of smoking habits ( $r = 0.29$  and  $0.50$ , respectively). Smoking habits of both sons and daughters correlated more highly with those of their fathers ( $r = 0.22$  and  $0.23$ , respectively) than with those of their mothers ( $r = 0.08$  and  $0.03$ , respectively).

Previously, we had not found a relationship between children's and parents' chronic symptoms by parental smoking (20). When we examined effects of parental smoking on children's pulmonary function, taking into account the initial relationship between parental and children's pulmonary function, only maternal smoking was a significant explanatory variable, and

only for  $\dot{V}_{max}$  ( $p = 0.043$ ). Considering the number of ways in which the comparisons were made, this one difference probably was not meaningful. When children's pulmonary function was adjusted for paternal body habitus as well as their own, there was no significant parental smoking contribution. A lack of a relationship between parental smoking and children's pulmonary function, even without correcting for parental pulmonary function or body habitus, had been reported by Speizer and coworkers (17, 18), Schilling and associates (10), and Dodge (12). Tager and colleagues (19) had reported this association, but it too might disappear if corrected for the family aggregation they found (9), and/or body habitus. It is possible that controlling for body habitus in a family may be controlling for other genetic and host factors as well.

Finally, we did not find any significant interaction between the smoking habits of either parent smoking and their spouses' lung function (table 3), similar to Comstock and coworkers (21) and Schilling and associates (10), but different from Kauffmann and coworkers (22).

#### References

1. Louis PCA. Recherches sur l'emphyseme des Poumons. Soc Med Obser Paris Mem 1837; 1:160-261.
2. Fuller HW. On disease of the chest including disease of the heart and great vessels. London: Churchill, 1862:296-8.
3. Morse J. Alpha<sub>1</sub>-antitrypsin deficiency. N Engl J Med 1978; 299:1045-8, 1099-1105.
4. Sibbald R, Turner-Warwick M. Factors influencing the prevalence of asthma among first degree relatives of extrinsic and intrinsic asthmatics. Thorax 1979; 34:332-7.
5. Sibbald R, Horn MEC, Gregg I. A family study of the genetic basis of asthma and wheezy bronchitis. Arch Dis Childhood 1980; 55:354-7.
6. Hankins D, Drage C, Zamel N, Krosenberg R. Pulmonary function in identical twins raised apart. Am Rev Respir Dis 1982; 125:119-21.
7. Hubert HB, Fabritz RR, Fienleib M, Caren G. Genetic and environmental influences on pulmonary function in adult twins. Am Rev Respir Dis 1982; 125:409-13.
8. Higgins M, Keller J. Familial occurrence of chronic respiratory disease and familial resemblance in ventilatory capacity. J Chronic Dis 1975; 28:239-51.
9. Tager IB, Rosner B, Tishler PV, et al. Household aggregation of pulmonary function and chronic bronchitis. Am Rev Respir Dis 1976; 114:483-92.
10. Schilling RSF, Letai AD, Hui SL, et al. Lung function, respiratory disease, and smoking in families. Am J Epidemiol 1977; 106:274-83.
11. Lebowitz MD, Knudson RJ, Burrows B. The Tucson epidemiology study of chronic obstructive lung disease. I. Methodology and prevalence of disease. Am J Epidemiol 1975; 102:137-52.
12. Dodge R. The effects of indoor pollution on Arizona children. Arch Environ Health 1982; 37:151-5.
13. Knudson RJ, Slatin R, Lebowitz MD, Burrows B. The maximum expiratory flow-volume curve: normal standards, variability, and the effects of age. Am Rev Respir Dis 1976; 113:587-600.
14. Oberman A, Lane NE, Mitchell RE, Greybiel A. The thousand aviator study monograph #12: distributions and intercorrelations of selected variables. Pensacola, FL: U.S. Naval Aerospace Medical Institute (PHS), 1965.
15. Donner A, Koval JJ. The estimation of intraclass correlation in the analysis of family data. Biometrics 1980; 36:19-25.
16. Townley R, Guirgis HA, Villacorte GV, et al. Methacholine sensitivity and atopic disease in asthmatic and non-atopic families. J Allergy Clin Immunol 1974; 53:107.
17. Speizer FE, Ferris B, Bishop YMM, Spengler J. Health effects of indoor NO<sub>2</sub> exposure: preliminary results. In: Lee SD, ed. Nitrogen oxides and their effects on health. Ann Arbor: Ann Arbor Science, 1980:343-59.
18. Speizer FE, Ferris B, Bishop YMM, Spengler J. Respiratory disease rates and pulmonary function in children associated with NO<sub>2</sub> exposure. Am Rev Respir Dis 1980; 121:3-10.
19. Tager IB, Weiss ST, Rosner B, Speizer FE. Effects of parental cigarette smoking on the pulmonary function of children. Am J Epidemiol 1979; 110:15-26.
20. Lebowitz MD, Burrows B. Respiratory symptoms related to smoking habits of family adults. Chest 1976; 69:48-50.
21. Comstock GW, Meyer MB, Helsing EJ, et al. Respiratory effects of household exposures to tobacco smoke and gas cooking. Am Rev Respir Dis 1981; 124:143-8.
22. Kauffmann F, Tessier JF, Oriol P. Adult passive smoking in the home environment: a risk factor for chronic airflow limitation. Am J Epidemiol 1983; 117:269-80.

2023379683

2023379684

Berwick, M., Zagraniski, R.T., Leaderer, B.P., Stolwijk, J.A.J.  
"Respiratory Illness in Children Exposed to Unvented Combustion  
Sources" Indoor Air: Radon, Passive Smoking, Particulates and  
Housing Epidemiology Volume 2: 255-260, 1984.

ABSTRACT. Using a staged design of air quality monitoring, we followed 174 families using unvented kerosene heaters and 173 families without heaters for a three-month period to evaluate the association between nitrogen dioxide (NO<sub>2</sub>) exposure and acute respiratory illness rates. Environmental and health data were obtained through personal interview, bi-weekly telephone interviews, tax assessor records, and from two-week integrated NO<sub>2</sub> measurements in 303 residences. One hundred-twenty-one children under age 13 were followed in this study, 59 living in homes with kerosene heaters and 62 living in homes without. Initial analyses indicate that exposed children have significantly more days of acute respiratory illness than controls. Limitations are imposed by sample size and by possible selection bias.

2023379685

# INDOOR AIR

Volume

**2**

## Radon, Passive Smoking, Particulates and Housing Epidemiology

Editors

**BIRGITTA BERGLUND**

Department of Psychology, University of Stockholm

**THOMAS LINDVALL**

Karolinska Institute and the  
National Institute of Environmental Medicine

**JAN SUNDELL**

National Board of Occupational Safety and Health

Swedish Council for Building Research  
Stockholm, Sweden 1984

REPRODUCED BY  
U.S. DEPARTMENT OF COMMERCE  
NATIONAL TECHNICAL  
INFORMATION SERVICE  
SPRINGFIELD, VA. 22161

2023379686

# **Proceedings of the 3rd International Conference on Indoor Air Quality and Climate**

**held in Stockholm  
August 20-24, 1984**

*Under the High Patronage of  
His Majesty King Carl XVI Gustaf*

**Organized by  
The Karolinska Institute and  
The National Institute of Environmental Medicine  
with the cosponsorship of  
The World Health Organization**

**Sponsored by**  
Commission of the European Communities  
Swedish Ministry of Health and Social Affairs  
U S Environmental Protection Agency  
Swedish Council for Building Research  
Swedish Work Environment Fund  
National Institute of Radiation Protection (Sweden)  
Representatives of European Heating and Ventilating Associations  
American Society of Heating, Refrigerating and Air-Conditioning Engineers  
Electric Power Research Institute (USA)  
Gas Research Institute (USA)  
Ruhrgas AG (FRG)  
Kawasaki Ltd (Japan)  
Drägerwerk AG (FRG)  
Fläkt AB (Sweden)  
Bahco AB (Sweden)  
Brüel & Kjær (Denmark)

2023379687

2023379688

INDOOR AIR

Volume 2

Radon, Passive Smoking, Particulates  
and Housing Epidemiology

## The 3rd International Conference on Indoor Air Quality and Climate

### Organizing committee

*Thomas Lindvall, M.D., Professor (President)*  
Karolinska Institute and National Institute of Environmental Medicine,  
Stockholm, Sweden

*Birgitta Berglund, Ph.D., Professor*  
Department of Psychology, University of Stockholm and Swedish Council  
for Research in the Humanities and Social Sciences, Stockholm, Sweden

*Jan Sundell, M.Sc.*  
National Board of Occupational Safety and Health, Stockholm, Sweden

### Overseas coordinators

*Professor Kazuo Maeda*  
Department of Epidemiology, University of Tokyo, School of Health Sciences,  
Tokyo, Japan

*Dr Demetrios Moschandreas*  
IIT Research Institute, Chicago, Illinois, USA

*Professor Bernd Seifert*  
Institute of Water, Soil and Air Hygiene, Berlin, Federal Republic of  
Germany

*Dr Peter Warren*  
Building Research Establishment, Watford, England

### Advisory committee

*Dr Ib Andersen*  
Danish National Institute of Occupational Health, Denmark

*Dr David R. Berg*  
U.S. Environmental Protection Agency, Washington DC, USA

*Dr Ulf Berglund*  
Royal Institute of Technology and National Institute of Environmental  
Medicine, Sweden

*Dr Irwin Billick*  
Gas Research Institute, USA

*Professor Trygg Engen*  
Department of Psychology, Brown University, USA

*Professor Povl Ole Fanger*  
Laboratory of Heating & Air Conditioning, Technical University of  
Denmark, Denmark

*Professor Benjamin Ferris Jr*  
School of Public Health, Harvard University, USA

*Professor Lars Friberg*  
Karolinska Institute and National Institute of Environmental Medicine,  
Sweden

2023379689



Professor Gideon Gerhardsen  
Swedish Employers Confederation, Sweden

Dr Anna Hambræus  
Institute of Clinical Bacteriology, University of Uppsala, Sweden

Dr Helmut Knöppel  
Joint Research Centre, Commission of the European Communities, Italy

Dr H W de Koning  
Division of Environmental Health, World Health Organization,  
Switzerland

Professor Michael D Lebowitz  
Health Science Center, University of Arizona, USA

Dr Anthony Nero  
Lawrence Berkeley Laboratory, University of California, USA

Professor Jan Stohr  
School of Medicine, Yale University, USA

Dr Ralph M Perdue  
Electric Power Research Institute, USA

Professor Eystein Rødahl  
Norwegian Institute of Technology, University of Trondheim, Norway

Dr John D Spengler  
School of Public Health, Harvard University, USA

Dr Michael Suess  
World Health Organization, Denmark

Professor James Woods Jr  
Engineering Research Institute, Iowa State University, USA

2023379690

# CONTENTS

	Page
<b>RADON IN DWELLINGS: EXPOSURE AND RISK ANALYSIS</b>	<b>13</b>
Nazaroff, W U Nero, A V	Transport of radon from soil into residences 15
Jonassen, N McLaughlin, J P	Airborne radon daughters, behavior and removal 21
Edling, C Wingren, G Axelsson, O	Radon daughter exposure in dwellings and lung cancer 29
<b>RADON: EXPOSURES AND RISKS</b>	<b>35</b>
Svedjemark, G A Mjones, L	Exposure to the Swedish population to radon daughters 37
Fenyves, E J Kinslow, R H	Indoor radon concentrations in public buildings 43
Put, L W de Meijer, R J	Survey of radon concentrations in Dutch dwellings 49
Papastefanou, C Manolopoulou, M Savvides, El Charalambous, St	Exposure from radon and radon daughters in dwellings 55
Brown, L Green, B M R Miles, J C H Wrixon, A D	Radon exposure of the UK population 61
Burkart, W Wernli, C Brunner, H	Assessment of additional exposures and risks from airtightening of homes in an Alpine area with high radon emanation 67
Pershagen, G Damber, L Falk, R	Exposure to radon in dwellings and lung cancer: A pilot study 73
Bergman, H Edling, C Axelsson, O	Indoor radon daughter concentrations and passive smoking 79
Wilson, C	Mapping the radon risk of our environment 85
Radford, E P St Clair Renard, K G	Application of studies of miners to radon problem in homes 93

2023379691

# RADON: SOURCES AND MEASUREMENT

Downard, T R Geiger, E L Millard, J B	Field evaluation of Eberline's radon daughter working level monitor	99
Orwald, R A Alter, H W	Localization of indoor radon sources using integrating track etch detectors	105
Paripas, B Takacs, S Somogyi, Gy Nikl, I	Integral alpha and gamma radiation measurements in dwelling houses	113
Schmied, H	The sensitivity to humidity of radon monitoring instruments	119
Gustafsson, J Nilsson, I	Tracing of radon leakages	125
Hawthorne, A R Gemmage, R B Dudney, C S	Effect of local geology in indoor radon levels: A case study	137
Kothari, B K	Contribution of soil gas, potable water, and building material to radon in US homes	143
Keller, C Folkerts, K H	A study on indoor radon	149
Jönsson, G	Radon measurements in Sweden. Some results	155
Martell, E A	Aerosol properties of indoor radon decay products	161

# FIBRES AND PARTICULATES IN THE INDOOR ENVIRONMENT

van Houdt, J J Boeleij, J S M	Mutagenic activity of indoor airborne particles compared to outdoors	169
Seifert, B Dreus, M Aurand, K	Indor heavy metal exposure of the population around a secondary lead smelter	177
Schneider, T	Man-made mineral fibers (MMF) and other fibers in the air and in settled dust	183
Sega, K Kalinic, M Sisovic, A	Indoor-outdoor relationships for respirable particles, total suspended particle matter and smoke concentrations in modern office buildings	189
McCarthy, S M Colome, S D Spengler, J D	Indoor and outdoor aerosols: A multivariate approach to source identification	195

2023379692

	9
<b>FIBRES AND PARTICULATES: CHARACTERIZATION AND RISKS</b>	<b>201</b>
Weechler, C J Fong, K L	Characterization of organic species associated with indoor aerosol particles 203
Meckler, M	Analysis of low particulate size concentration levels in office environments 209
Janka, K Kulmala, V	Optical particle counter as a wide range, continuous monitor for particle concentrations 215
Rindel, A	Man-made-mineral fibres (MMMF) in indoor climate 221
Gunnarsson, M Bergström, B	Are man-made mineral fibres responsible for the development of bronchitis and atelectasis of the lung? 225
Tockman, M S Wheeler, P Frost, J K Ball Jr, W Levin, M Green, K	Pleural changes consistent with asbestos exposure found on screening radiographs are not predictive of lung cancer 229
<b>EPIDEMIOLOGICAL STUDIES OF HEALTH DISORDERS RELATED TO HOUSING</b>	<b>235</b>
Iversen, M Bach, E Lundqvist, G R	A prospective study of the health and comfort changes among tenants after retrofitting of their flats 237
Matsuki, H Yanagisawa, Y Osaka, F Kasuga, H Nishimura, H	Personal exposure to NO <sub>2</sub> and its health effect with urinary hydroxyproline to creatinine ratio as biochemical indicator 243
Valbjörn, O Kousgård, M	Headache and mucus membrane irritation. An epidemiological study 249
Bervick, M Zagraniiski, R T Leaderer, B P Stolwijk, J A J	Respiratory illness in children exposed to unwanted combustion sources 255
Lets, R Quackenbush, J J Spengler, J D	Effects of choice of exposure index in NO <sub>2</sub> epidemiological studies 261

2023379693

		10
HOUSING EPIDEMIOLOGY		267
Goldstein, I Hartel, D Andrews, L	Indoor exposure of asthmatics to nitrogen dioxide	269
Loewenstein, J C Bourdel, M C Maffiolo, G Krainik, P Wolmark, Y	Relation of environmental conditions to the health of the elderly in a long term care hospital: A longitudinal survey	275
Mage, D T	A possible relationship of sudden infant death syndrome to indoor air quality	281
Speizer, F E Ware, J Dockery, D Ferris Jr, B G	Lack of effect of gas stoves on longitudinal change in lung function in children ages 6-11 years	287
PASSIVE SMOKING AND HEALTH EFFECTS		295
Weber, A	Environmental tobacco smoke exposure: acute effects - acceptance levels - protective measures	297
Schmidt, P	Passive smoking as a real risk to health	303
Ferris Jr, B G Dockery, D W Ware, J H Berkey, C S Speizer, F E	Effects of passive smoking on children in the six-cities study	309
Hoffmann, D Brunnemann, K D Adams, J D Malley, M J	Indoor air pollution by tobacco smoke: Model studies on the uptake by nonsmokers	313
Hugod, C	Passive smoking - a source of indoor air pollution	319
PASSIVE SMOKING: CHARACTERIZATION AND COUNTERMEASURES		327
Sterling, T D	Effects of restricting and prohibiting smoking in office environments on reactions of office personnel to environmental health and stress factors	329
Matsushita, H Mori, T	Nitrogen dioxide and nitrosamine levels in indoor air and side-stream smoke of cigarette	335

2023379694

		11
Lehti, H	Ashtray	341
Vertio, H		
Ramström, L M	Smokers' and non-smokers' perception of passive smoking and certain control measures	345
Winnika, G	Patterns and determinants of reaction to tobacco smoke in an experimental exposure setting	351
Plischka, K		
Roscovanu, A		
Schlipkoeter, H W		

2023379695

RESPIRATORY ILLNESS IN CHILDREN EXPOSED TO  
UNVENTED COMBUSTION SOURCES

Marianne Berwick, Rebecca T. Zagraniski\*, Brian P. Leaderer\*\*, and  
Jan A. J. Stolwijk\*\*

Dept. Epidemiology and Public Health, Yale University  
School of Medicine, New Haven, CT 06510, USA

\*New Jersey Department of Health, Trenton, NJ 08625, USA

\*\*Dept. Epid. and Pub. Hlth., Yale Univ. School of Medicine and  
J.B. Pierce Found. Lab., New Haven, CT 06510, USA

NOTICE  
This material may be  
protected by copyright  
law (Title 17 U.S. Code)

Abstract

Using a staged design of air quality monitoring, we followed 174 families using unvented kerosene heaters and 173 families without heaters for a three-month period to evaluate the association between nitrogen dioxide (NO<sub>2</sub>) exposure and acute respiratory illness rates. Environmental and health data were obtained through personal interview, bi-weekly telephone interviews, tax assessor records, and from two-week integrated NO<sub>2</sub> measurements in 303 residences. One hundred-twenty-one children under age 13 were followed in this study, 59 living in homes with kerosene heaters and 62 living in homes without. Initial analyses indicate that exposed children have significantly more days of acute respiratory illness than controls. Limitations are imposed by sample size and by possible selection bias.

Introduction

Unvented combustion in homes can lead to high ambient levels of several air contaminants with nitrogen dioxide (NO<sub>2</sub>) being the most notable (1). While NO<sub>2</sub> has been implicated as a potentiator of lower respiratory infections in laboratory animals (2), the epidemiologic evidence for determining unhealthy levels in humans is inconclusive at this time. Melia *et al.* (3,4) and Florey *et al.* (5) have reported data that suggest that children between the ages of 5 and 11 living in homes with gas cooking stoves had higher levels of acute respiratory symptoms or disease than those living in homes with electric cooking stoves. The range of NO<sub>2</sub> exposures measured in these studies was from 8-634 µg/m<sup>3</sup>. The generalizability of these studies is limited by low

2023379696

response rates and an overrepresentation of lower socioeconomic status groups.

Keller *et al.* (6,7) found no difference in illness rates between volunteers who lived in homes using gas for cooking and those using electricity. The range of  $\text{NO}_2$  exposures in their study was reported for a sample of homes only and was very low ( $22 \text{ ug/m}^3$ ), so that it was unlikely that any positive association could be found. The potential for recall bias limits the finding of Speizer *et al.* (8) that children living in homes with gas cooking stoves had higher respiratory illness rates before age two than children living in homes using electricity stoves. Dodge (9) reported that exposure to parental smoking and gas cooking was associated with higher respiratory symptom rates in Arizona schoolchildren. However, his sample is unrepresentative, suffered from low response rates, and no pollutant measures were made.

The investigation reported here was designed to determine whether exposure to air contaminants emitted by kerosene space heaters, particularly  $\text{NO}_2$ , is associated with excess respiratory illness in children. We hypothesized that there was a positive correlation between  $\text{NO}_2$  levels and acute respiratory illness rates among children. We identified a population with kerosene heaters where we could measure the household  $\text{NO}_2$  exposures of children while accounting for many of the other potential risk factors for respiratory infections, such as parental smoking, presence of gas appliances, household size, school attendance, socioeconomic status, age, and previous history of respiratory infections.

#### Methods

Study Design and Population. To allow the most precise yet efficient estimation of individual exposures to pollutants, a staged design of air quality monitoring was employed in a cohort study. A cohort of adults who bought kerosene heaters was identified from lists obtained from local kerosene heater dealers in Connecticut. A control household was systematically chosen from the neighborhood of an exposed household. Neighborhood controls were selected to control ambient air quality and socioeconomic status. In each household an index woman, the oldest woman residing in the house, and an index child (if a child lived in the house), the child nearest in age to 5 but less than 13, were chosen to participate in the study. Households with no adult female present and households no longer using kerosene heaters were excluded from the study.

If subjects agreed to participate, an initial questionnaire was administered. Information was obtained about building characteristics, user heating patterns, and the health history and current respiratory symptomatology of the index adult and the index

2023379697



child (if present). Subjects were then followed up by telephone bi-weekly for 12 weeks during January-March 1983 to obtain respiratory symptoms for the female and the child (if present) and heater use patterns during the previous two weeks period. As described in a separate paper (10) air monitoring for  $\text{NO}_2$  was conducted for at least one two-week period in 87.3 percent of the study households. The study population analyzed here consists of 121 children under age 13. Fifty-nine lived in homes with kerosene heaters; 62 lived in homes without. All children were Caucasian.

**Definition of Variables.** The independent variables used in these analyses included: (1) demographic factors: age, sex, socioeconomic status [SES, Hollingshead Index(11)]; (2) exposure parameters: number of minutes of gas cooking per day (total estimated oven and burner use), number of cigarettes normally smoked daily at home by all residents, school enrollment, type of cooking fuel, total household size (a proxy for density), average daily hours of kerosene heater use for each two-week period, one two-week average measurement of  $\text{NO}_2$  in each residence, and (3) respiratory illness history. "Respiratory illness history" was a continuous variable derived by adding each serious respiratory disease reported in the initial questionnaire (i.e. ever had pneumonia) and the average number of chest colds per year (estimated by the mother).

We used the reported average hours of kerosene heater use during each two-week period as a proxy for  $\text{NO}_2$  exposure. Average hours of heater use (by household) correlates fairly well with integrated average  $\text{NO}_2$  measurements ( $r = 0.70$ ,  $p < 0.001$ ). The variable, average hours of heater use, was available for each child for each of 6 periods.

The dependent variable used in multivariate analysis, days of illness, was not normally distributed, so we dichotomized it as one or more days of illness and no days of illness and used linear logistic regression following the methods of Harrell (12). SAS 82.3 programs were used for nonparametric analyses and the linear logistic regression. For variables that were normally distributed (i.e. age, household size, etc.), we computed means, t-tests, and correlations using StatPac (13) on the IBMPC.

### Results

**Participation and Demographic Factors.** The household participation rate among the exposed group was 77.9 percent and 80.7 percent among the unexposed. The loss to follow-up over the study period was 3.4 percent among the exposed group and 5.7 percent among the unexposed.

There were no statistically significant demographic differences

between the exposed and unexposed groups of children. The mean age of the children studied was 6.8 years, the mean household size was 4.2 persons per household, the mean index of SES was 43.4, and the mean index of history of respiratory illness was 2.7.

**Exposure Factors.** There was more gas cooking in the unexposed children's homes (46.5 minutes/day) when compared to the exposed children's (17.5 minutes/day),  $t$ -test=1.82,  $p$  = 0.07, two-tailed; however, since so few children's homes had gas stoves (8 exposed, 13 unexposed), there were not enough data for meaningful use in the present analysis. There was no statistically significant difference in the mean number of cigarettes smoked daily in children's homes (12.63 exposed, 12.74 unexposed). Average two-week integrated  $\text{NO}_2$  samples were taken in 113 of the 121 children's homes in four places: outdoors, in the kitchen, in a living room, and in an adult's bedroom. The mean outdoor level of  $\text{NO}_2$  for exposed households was 14.62  $\mu\text{g}/\text{m}^3$  (range 5-43  $\mu\text{g}/\text{m}^3$ ) and 12.70  $\mu\text{g}/\text{m}^3$  (range 0-26  $\mu\text{g}/\text{m}^3$ ) for unexposed households. The mean kitchen level of  $\text{NO}_2$  in homes with kerosene heaters was 46.92  $\mu\text{g}/\text{m}^3$  (range 3-211  $\mu\text{g}/\text{m}^3$ ) and 14.07  $\mu\text{g}/\text{m}^3$  (range 0-80  $\mu\text{g}/\text{m}^3$ ) in homes without kerosene heaters. The mean living room level of  $\text{NO}_2$  in children's homes with kerosene heaters was 46.84  $\mu\text{g}/\text{m}^3$  (range 3-154  $\mu\text{g}/\text{m}^3$ ) and 10.36  $\mu\text{g}/\text{m}^3$  (range 0-63  $\mu\text{g}/\text{m}^3$ ) in children's homes without kerosene heaters. The mean level of  $\text{NO}_2$  found in bedrooms in exposed homes was 46.82  $\mu\text{g}/\text{m}^3$  (range 3-225  $\mu\text{g}/\text{m}^3$ ) and 10.4  $\mu\text{g}/\text{m}^3$  (range 0-66  $\mu\text{g}/\text{m}^3$ ) in bedrooms in unexposed homes. The overall average use of kerosene heaters was 7.7 hours per day (range 0-24 hours per day).  $\text{NO}_2$  measurements in children's homes with kerosene heaters were on average 3-4 times as high as in homes without heaters.

**Association between exposure and acute respiratory illness.**

First, in order to determine whether kerosene heater exposure had an association with the days of illness, nonparametric statistical tests were applied to the data. Children exposed to kerosene heaters and children not exposed to heaters were ranked as to the total number of days sick over the 12 week follow-up period. A Wilcoxon rank sum test was performed using the  $t$ -approximation for the significance levels. Children living in homes with kerosene heaters had significantly more days of illness than children living in homes without kerosene heaters ( $z=2.14$ ,  $p$  < 0.05).

Next, rank correlations were carried out between all independent variables and the dependent variable, days of illness. There was little association between average hours of heater use and number of days sick over the entire period (Spearman correlation coefficient,  $r_s$  = 0.06,  $p$  = 0.09). Age and history of respiratory illness were more strongly associated with days of illness ( $r_s$  = 0.344,  $p$  < 0.01  $r_s$  = -0.17,  $p$  < 0.05, respectively).

Finally, linear logistic regression was used to determine which variables were significantly associated with one or more days of

2023379699

illness during each two-week period while adjusting for other measured potential risk factors. Average hours of heater use per day were significantly associated with days of illness ( $p < 0.05$ ) while controlling for type of cooking fuel, cigarettes smoked per day, household size, sex, age, school enrollment, and history of respiratory illness. Age had a significant, inverse association with days of illness ( $p < 0.05$ ). History of respiratory illness was positively associated ( $p < 0.05$ ). SES was marginally associated ( $p = 0.07$ ).

#### Discussion

This initial analysis suggests that young children with a history of respiratory infections are the most sensitive to the adverse health effects of  $\text{NO}_2$  (or kerosene heater exposure). These results are consistent with previous studies that have shown that exposure to gas cooking has no effect on respiratory illness in women and school-age children (6,7), a borderline association with 5-11 year-olds (2,3,4) and an association with the history of respiratory illness in children under 2 years(7). The effects seem to be the most pronounced in young age groups. It should be emphasized that the results presented are preliminary.

These data are subject to many potential biases, some of which are: [1] recall bias in terms of reporting appliance use; [2] a limited ability to generalize from a convenience sample; [3] the publicity surrounding the safety of kerosene heaters; [4] all heater-owners had operated their heaters for at least one season prior to the study; as many as 34 potentially sensitive people were not eligible because they no longer used their heaters due to odor or hypersensitivity. A final limitation is the small sample size.

Further research should concentrate on studying the association between  $\text{NO}_2$  exposure and younger-aged children.

Acknowledgements. The authors would like to gratefully acknowledge the constant support of Diane Goudreau, head interviewer, and the statistical advice of Ted Holford. This research was aided by a Grant-in-Aid of Research from Sigma Xi, and N.I.H. grants ES-07085 and ES-00354.

#### References

- (1) Leaderer, B.P. Air pollutant emissions from kerosene space heaters. *Science*, 1982, 218, 1113-1115.

2023379700

- (2) Ehrlich, R. Effect of air pollutants on respiratory infections. Arch. Env. Hlth. 1962, 6:638-642.
- (3) Melia, R.J.W., C. du V. Florey, D.G. Altman, and A.V. Swan. Association between gas cooking and respiratory disease in children. Brit. Med. J. 1977 (2):149-152.
- (4) Florey, C. du V., R.J.W. Melia, S. Chinn, B.D. Goldstein, A.G.F. Brooks, H.H. John, I.B. Craighead, and X. Webster. The relation between respiratory illness in primary schoolchildren and the use of gas for cooking III. Nitrogen dioxide, respiratory illness and lung function. Int. J. Epid. 1979, 8:347-353.
- (5) Melia, R.J.W., C. du V. Florey, R.W. Morris, B.D. Goldstein, H.H. John, D. Clark, I.B. Craighead, and J.C. Mackinlay. Childhood respiratory illness and the home environment II. Association between respiratory illness and nitrogen dioxide ( $\text{NO}_2$ ), temperature and relative humidity. Int. J. Epid. 1982, 11:164-169.
- (6) Keller, M.D., R.R. Lanese, R.I. Mitchell, and R.W. Cote. Respiratory illness in households using gas and electricity for cooking. I. Survey of incidence. Env. Res. 19, 495-503 (1979).
- (7) Keller, M.D., R.R. Lanese, R.I. Mitchell, and R.W. Cote. Respiratory illness in households using gas and electricity for cooking. II. Symptoms and objective findings. Env. Res. 19, 504-515 (1979).
- (8) Speizer, F.E., B. Ferris, Jr., Y.M.M. Bishop, and J. Spengler. Respiratory disease rates and pulmonary function in children associated with  $\text{NO}_2$  exposure. Am. Rev. Resp. Dis. 121, 1980, 3-10.
- (9) Dodge, R. The effects of indoor pollution on Arizona children. Arch. Env. Hlth. 1982, 37:151-155.
- (10) Leaderer, B.P., R.T. Zaganiski, N. Berwick, J.A.J. Stolwijk, and Q.S. Ma. Residential exposure to  $\text{NO}_2$ ,  $\text{SO}_2$ , and  $\text{HCHO}$  associated with unvented kerosene space heaters, gas appliances and sidestream tobacco smoke. Proc. 3rd Intern. Conf. Indoor Air Quality and Climate, Stockholm 1984.
- (11) Hollingshead A.B. Two factor index of social position, New Haven, Ct: August B. Hollingshead Publications, 1957.
- (12) Harrell F. E. The logist procedure. SAS Supplemental Library User's Guide, 1980 Edition. SAS Institute, N.C. 1980.
- (13) Walonick, D.S. 1983. Statpac: Statistical analysis system for the IBMPC. Minneapolis, MI.

2023379701

2023379702

Gardner, G., Frank, A.L., Taber, L.H. "Effects of social and family factors on viral respiratory infection and illness in the first year of life" Journal of Epidemiology and Community Health 38: 42-48, 1984.

ABSTRACT. A total of 131 infants were monitored from birth through the first year of life for respiratory viral infection and illness and evaluated for the relationship that these had to certain social and familial factors. The results showed no general patterns of association between viral infection and the study factors, but there were several significant individual associations. Excess influenza virus infection was found for black infants, infants with at least one sibling, and especially those with school age siblings. Rhinovirus infection rates were highest among girls attending daycare. In addition, significantly higher rates of lower respiratory disease (LRD) were seen in daycare infants and low socioeconomic infants and a definite trend to increasing amounts of LRD was seen with increasing family size. Protection from LRD seen in girls was apparently lost in daycare. No convincing differences for viral infection or respiratory illness were seen with parental smoking as an isolated factor.

2023379703

# NOTICE

This material may be  
protected by copyright  
law. (Title 17 U.S. Code).

*Journal of Epidemiology and Community Health*, 1984; 38, 42-48

MARCH (1)

## Effects of social and family factors on viral respiratory infection and illness in the first year of life

GREGORY GARDNER,<sup>1</sup> ARTHUR L FRANK,<sup>1,2</sup> AND LARRY H TABER<sup>1</sup>

*From the Influenza Research Center,<sup>1</sup> Department of Microbiology and Immunology, and Myers-Black<sup>2</sup> Infectious Diseases Section,<sup>2</sup> Department of Pediatrics, Baylor College of Medicine, Houston, Texas, USA*

**SUMMARY** A total of 131 infants were monitored from birth through the first year of life for respiratory viral infection and illness and evaluated for the relationship that these had to certain social and familial factors. The results showed no general patterns of association between viral infection and the study factors, but there were several significant individual associations. Excess influenza virus infection was found for black infants, infants with at least one sibling, and especially those with school age siblings. Rhinovirus infection rates were highest among girls attending daycare. In addition, significantly higher rates of lower respiratory disease (LRD) were seen in daycare infants and low socioeconomic infants and a definite trend to increasing amounts of LRD was seen with increasing family size. Protection from LRD seen in girls was apparently lost in daycare. No convincing differences for viral infection or respiratory illness were seen with parental smoking as an isolated factor.

Viral respiratory illness is a major cause of morbidity and mortality in infancy. Children under 1 year of age have the highest incidence of acute respiratory illness<sup>1-4</sup> and most are apparently caused by viruses.<sup>5</sup>

Social and family factors influence the incidence of illness during infancy<sup>6-8</sup> but documented infection rates have been less frequently studied. For this reason we examined both infection and illness during the first year of life of 131 infants followed up in the Houston Family Study between 1975 and 1980.

### Materials and methods

#### RECRUITMENT AND MONITORING

General methods used in the Houston Family Study have been reported previously.<sup>9-11</sup> A total of 131 infants were observed for the first year of life from 1975 to 1980. In 1975-6 recruitment of pregnant women took place at Jefferson Davis, a county hospital; thereafter all recruiting was from the community at large at an average of two or three families a month. The infants had blood obtained at birth (cord blood) and at 4, 8, and 12 months of age. Home visits were made every week during the respiratory virus season (biweekly at other times) for history and physical examination and to obtain nasal wash specimens for virus culture from infants. Additional home or clinic visits were made as needed

for sampling of all illnesses. Diagnoses were made by a physician, nurse, or physician's assistant.

Records of all clinical contacts were available for review of illnesses. Upper respiratory illnesses (URI) were categorised as afebrile, febrile, or otitis media. For lower respiratory disease (LRD), the categories were laryngotracheobronchitis (LTB), bronchiolitis, or pneumonia. On review, illnesses lasting more than two weeks could usually be reinterpreted as two or more illnesses. When difficulty arose as to the nature or duration of an illness, the impressions of people seeing the child during the illness were used.

#### LABORATORY METHODS

Tissue cultures used for virus isolation were rhesus monkey kidney, MDCK, LLC-MK2, HEP-2, and WI-38.<sup>12-14</sup> Some specimens were inoculated into fertilised hen's eggs.<sup>15</sup> Serological tests included haemagglutination inhibition for influenza A and B<sup>16</sup> and microneutralisation for respiratory syncytial virus (RSV), parainfluenza virus types 3 (para 3),<sup>17</sup> and influenza A and B.<sup>18</sup> Fourfold rise in antibody titre (or failure of passively acquired antibody to fall) was considered evidence of infection.

#### SOCIAL AND FAMILY FACTORS

Personal and family data were obtained on enrolment and then recorded for each subsequent

year. Six factors were studied: sex, race, parental smoking, socioeconomic class, number of siblings, and attendance at daycare. Race was white or non-white with the latter including blacks and Mexican-Americans. An infant was considered exposed to parental smoking if either mother or father or a live-in relative smoked five or more cigarettes a day. An infant was considered a daycare attender if attendance at a daycare facility or mother's day out (sponsored by local churches) was consistent for at least five months. Finally, socioeconomic class was "low" if the family was eligible for the county hospital or made less than \$12 000 a year, "medium" if the family had private medical insurance or made more than \$12 000 a year, and "high" if the family had private medical insurance, made more than \$12 000 a year, and one or both parents had attended at least three years of college.

#### ANALYSIS

Viral infection and respiratory illness rates were analysed for each family factor category. The mean number of infections or illnesses was calculated from the total number of episodes and reported as the rate per 100 child years. Chi-square analysis was done on the distribution of the data.

#### Results

From 1976 to 1980, 92 infants (including three sets of twins) from 75 families were followed up. There were 59 whites, 24 blacks, and nine Mexican-Americans. Forty two per cent of the black and Mexican-American families were in the low socioeconomic group compared with 15% of the white families. The 39 infants studied from spring 1975 to spring 1976 will be included in selected analyses only because of socioeconomic imbalance (38 of 39 in low socioeconomic class) and some limitation in detailed clinical information on minor or non-influenza A illnesses, or both, during this first study year. This group was composed of 13 white, 21 black, and five Mexican-American infants.

#### VIRUS INFECTION

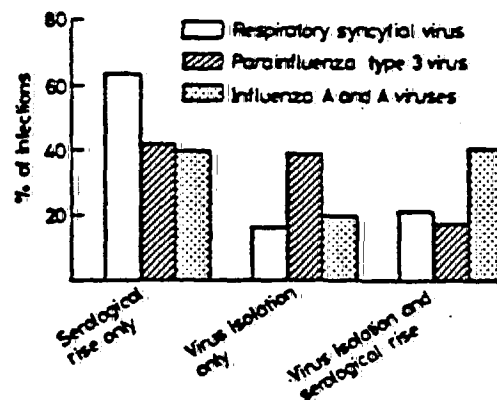
The figure shows the number of infections documented for the four viruses where serology was used in addition to virus isolation. Respiratory syncytial virus (RSV) had the largest proportion of infections identified by serological methods alone (63%). Of 40 influenza A and B infections (35 type A and five type B), 40% were identified by serology alone. In addition, 42% of the parainfluenza type 3 (para 3) infections were identified by serology alone. The remainder of the infections shown in tables 1 and 2 for these four agents were identified by isolation alone or isolation plus fourfold serological rise.

Table 1 shows the virus infection according to the selected social and family factors. In general, these factors were not significantly related to rates of proved viral infection. There were, however, some interesting exceptions.

Adenovirus infection rates were significantly associated with the number of siblings and daycare attendance. Infants with one sibling had the highest rate of infection while those with no siblings had the lowest. Infants with one sibling more often attended daycare (41%) when compared with those with none or two or more sibling infants (19% and 15% respectively); this may have influenced the chi square results. Numbers became too small when further analyses of daycare by number of siblings was done for adenovirus infection so the influence of the two factors could not be separated.

Both sex and daycare attendance were significantly associated with rhinovirus infection. Girls attending daycare had a much higher rate of rhinovirus infection (169) than did boy daycare attenders (50) or all infants not in daycare (48). In addition, 54% of girl daycare attenders had multiple infections compared with 20% of the boys; 77% of girls in daycare had had at least one infection compared with 53% for all infants combined.

Seventy four per cent of low socioeconomic class infants had had at least one para 3 infection compared with 47% for medium socioeconomic class and 54% for high, and this is reflected in the trend (not significant) in overall infection rates. None of the viruses considered was significantly associated with parental smoking for 1976-80. A significant relationship was found only for RSV and smoking mothers at home ( $p=0.020$ ) when 1975-6 data were included.



Evidence of respiratory syncytial, parainfluenza type 3, and influenza A and B virus infection in study infants, Houston Family Study 1975-80. Serological rise included failure of fall of passively acquired maternal antibody.

2023379705



Table 1 Virus infection rates per 100 child years for 131 infants according to sex, race, smoking, number of siblings and daycare: Houston Family Study, 1976-80.

Virus	Sex		Race		Socioeconomic class			Parental smoking		No of siblings			Daycare	
	Male (n=47)	Female (n=45)	White (n=59)	Non-white (n=33)	Low (n=23)	Medium (n=21)	High (n=48)	Yes (n=37)	No (n=35)	0 (n=37)	1 (n=29)	>2 (n=26)	Yes (n=23)	No (n=49)
Respiratory syncytial virus	64	84	73	76	74	76	73	78	71	73	79	69	78	72
Parainfluenza type 3	70	58	57	70	67	57	56	70	60	63	65	65	61	63
Influenza A and B	26	24	17	39*	35	19	23	22	27	11	34	31	23	26
Parainfluenza types 1 and 2	16	13	12	12	9	14	12	13	11	3	23†	15	17	10
Adenoviruses	28	24	32	30	26	33	33	32	31	14	22‡	35	32§	25
Rotavirus unclassified	26	29	25	21	21	24	23	24	23	24	27	15	13	24
Rhinoviruses	44	84¶	61	70	56	67	66	49	74	48	76	72	117¶	48
Enteroviruses	62	58	59	61	56	42	50	46	69	57	59	63	46	64
Total virus infection	340	374	356	379	404	332	334	334	346	292	413	367	404	334

\* $\chi^2=4.38$ ,  $p=0.034$ .† $0 < 1$ ,  $\chi^2=5.55$ ,  $p=0.018$ .‡ $\chi^2=8.17$ ,  $p=0.017$ ,  $0 < 1$ ,  $p=0.005$ ,  $0 < 2$ ,  $p=0.045$ .§ $\chi^2=3.05$ ,  $p=0.023$ .¶ $\chi^2=16.05$ ,  $p=0.003$ .¶ $\chi^2=16.86$ ,  $p=0.002$ .

Table 2 Respiratory illness rates per 100 child years for 131 infants according to sex, race, smoking, number of siblings, and daycare: Houston Family Study 1976-80.

Illness	Sex		Race		Socioeconomic class			Parental smoking		No of siblings			Daycare	
	Male (n=47)	Female (n=45)	White (n=59)	Non-white (n=33)	Low (n=23)	Med (n=21)	High (n=48)	Yes (n=37)	No (n=35)	0 (n=37)	1 (n=29)	<3 (n=26)	Yes (n=23)	No (n=49)
Acute URI	540	580	564	588	600	328	534	565	556	451	613	619	626	537
Pediatric URI	164	160	149	188	165	190	190	157	167	135	213	146	222	143
Ortic media	78	46	68	34	82	32	58	65	62	69	34	37	74	39
Total URI	783	787	761	830	847	770	762	787	785	655	880	822	922	719
LTB	62	42	54	42	78*	71	31	35	63	43	45	69	46	33
Bronchitis	45	33	39	39	56	30	39	40	36	23	48	30	61	32
Pneumonia	2	9	3	9	8	9	3	9	4	5	6	4	13	3
Total LRD	109	83	100	90	143†	110	72	84	103	71	99	123	122‡	68
Total respiratory illness	893	870	861	920	990	870	834	871	891	726	979	945	1044	827

\* $\chi^2=11.30$   $p=0.023$  low + high  $p=0.006$  med + high  $p=0.062$ .†Low + high  $\chi^2=8.74$   $p=0.032$ .‡ $\chi^2=10.67$   $p=0.014$ .

URI = Upper respiratory illness.

LTB = Laryngotracheobronchitis.

LRD = Lower respiratory disease.

Table 1 shows that influenza A and B infection rates varied significantly with race. Data for 1975-6 influenza A and B infections were combined with the 1976-80 data because surveillance of the influenza A/Victoria epidemic that occurred was comparable with later years (table 3). The significant association

with race was also seen in 1975-80. In addition, significant associations were found for race and influenza A only ( $p=0.008$ ). Seventy three per cent of these black infants had one or more siblings (1975-80) compared with 56% of white, but for 1976-80 this was reversed (black 41% white 53%).

2023379706

### Social factors and respiratory viruses

Table 3. Influenza A and B infection rate per 100 child years according to selected social and family factors, 1975-80

	No	Influenza A & B infection rate
Sex: Boy	67	27
Girl	64	24
Race: White	72	19
Other	29	44*
Socioeconomic class:		
Low	61	41
Medium	22	18
High	45	23
Parental smoking:		
Yes	66	33
No	63	27
No of siblings:		
0	49	18
1	41	32
≥2	41	44†
Daycare:		
Yes	30	33
No	101	30

\* $p=0.14$ ,  $p=0.004$ , influenza A only,  $p=0.036$  black v white,  $p=0.008$ .

† $p=0.97$ ,  $p=0.030$ , influenza A only,  $p=0.013$  0 v ≥2  $p=0.008$ .

Influenza A and B infection was also significantly related to number of siblings as was influenza A alone ( $p=0.013$ ). A stronger association was seen when comparing none with two or more siblings ( $p=0.008$ ). These relationships with number of siblings were not seen with the 1976-80 data only.

Independence between race and number of siblings for low socioeconomic infants was suggested by analysing all three factors simultaneously. There was a trend towards increase in the rate of infection with number of siblings for both white and non-white in the low socioeconomic group; non-white infants had higher rates compared with white in each sibling category. This was not seen in any other socioeconomic group or for the data as whole. Most influenza A and B infections (25/40), however, occurred in the low socioeconomic infants (mostly due to the A/Victoria epidemic of 1975-6) and numbers were too small in other comparisons. Regardless of how the data were grouped, all analyses comparing infants with no siblings with infants with one or two or more siblings showed lower rates of infection in those without siblings. In addition to the association with number of siblings, 70% of infants with two or more siblings had at least one school aged sibling, whereas for those with only one, the sibling tended to be of preschool age (15% school aged). During the epidemic of 1975-6, 38% of

the study infants had evidence of infection and 80% of these had school age siblings.

### RESPIRATORY ILLNESS

Respiratory illness rates are shown in table 2 according to the selected social and family factors. In general, the significant relationships and interesting trends found were in the area of more severe illness. As shown in the first two columns of table 2, boys had higher rates of illness in several of the diagnostic categories but none of these trends was significant. The rate of total LRD varied significantly with both socioeconomic class (low v high only) and daycare attendance, and a similar trend was noted with increasing number of siblings. There were indications that all three factors may affect total LRD independently. The larger families were distributed almost equally among all three socioeconomic classes, although low and medium classes had higher percentages of families with two or more siblings (low 39%, medium 38%, high 19%). Rates of total LRD for infants with two or more siblings were found to be highest in low socioeconomic families (166 per 100 child years) and lowest in high socioeconomic class families (80 per 100 child years). Also the low socioeconomic families were the least likely to send their infants to daycare. Only 13% of low socioeconomic infants were in daycare compared with 28% of the medium and 35% of the high socioeconomic class infants.

Rates of total LRD for girls and boys not attending daycare were 69 and 105, respectively, while girl and boy infants attending daycare had rates of 123 and 120. Rates of bronchiolitis and pneumonia were essentially equal for both sexes in daycare.

A statistically significant variation in the rate of LTB (a component of LRD) was also found in all three socioeconomic classes, but separate analysis of medium v high was found not to be significant ( $p=0.062$ ).

No statistically significant relationship was seen between total respiratory illness and parental smoking for the 1976-80 infants. Nevertheless, data on severe illnesses in 1975-6 were comparable with later years, and all six episodes of pneumonia that year occurred in infants of mothers who smoked. Overall, from 1975 to 1980 there were 11 episodes of pneumonia and nine (82%) occurred in black infants of mothers who smoked. The highest rate of pneumonia (25) was found in infants with non-employed mothers who smoked and this compared with a rate of 1.5 in those with non-employed mothers who were non-smokers ( $p=0.001$ ).

2023379707

and still found a higher rate of LRD among infants of low socioeconomic class even when controlled for family size (although numbers were small) and despite the fact that few of these infants were in daycare. Factors other than medical care or family size seem to be important influences on the incidence of LRD in the low socioeconomic infants. Trends to more infection and illness in general were present in this group.

Past studies have implicated daycare attendance as a cause of increased respiratory illness in children, especially infants. Strangert and Loda *et al* noted this in infants aged 6-15 months and under 12 months old, respectively.<sup>27,28</sup> Vihma found annual illness rates in daycare compared with home to be 6.3 v 2.5.<sup>29</sup> These results are in agreement with our findings. In addition, we found that girl infants in daycare seem to lose the relative "protection" from LRD observed for girl infants at home. Rates of serious lower respiratory disease—that is, bronchiolitis and pneumonia—were equal in boy and girl daycare attenders.

Infants of parents who smoked in our study were not at greater risk for viral infection or respiratory illness and even had a lower rate of LTB. The only exception to this was a significant relationship between pneumonia and parental smoking (especially mothers at home who smoked) only evident when the 1975-6 data were included. This effect could not be separated from the influence of race or socioeconomic class. Our observations are in contrast with those of Harlap and Davies<sup>30</sup> and Leeder *et al*.<sup>3</sup> Both studies found a highly significant relationship between passive smoking and lower respiratory illness, specifically bronchitis and pneumonia. Methods in these studies differed considerably from our own; Harlap and Davies used data from large numbers of infants in hospital whereas Leeder *et al* followed up a cohort of children by means of yearly questionnaires. Although the total number of episodes of LRD (112 including 1975) experienced by the infants in our study was small by comparison (especially pneumonia), ascertainment was more direct and illnesses were well documented.

We are grateful to Janet Wells, PAC, and her predecessors for making the Houston Family Study possible. Dr Abel Paredes participated in the study, 1975-7. Excellent management of the manuscript was provided by Kay Brown. Supported by contracts AI-92611 and AI-22672 and grant USPHS-MO1-RR-0188 (Clinical Research Center) from the National Institutes of Health. Computational assistance was provided by the Clinco project funded by the Division of Research Resources of the NIH grant number RR-00350.

## References

- <sup>1</sup>Monto AS, Ross H. Acute respiratory illness in an American community, the Tecumseh study. *JAMA* 1974; 227: 164-9.
- <sup>2</sup>Glezen WP, Loda FA, Clyde WA Jr, *et al*. Epidemiologic patterns of acute lower respiratory disease of children in a pediatric group practice. *J Pediatr* 1971; 78: 397-406.
- <sup>3</sup>Backstrom-Sarvinen L, Tsaala R, Kantero RL, Hallman N. Illness among normal Finnish children during the first five years of life. *Annales Paediatricae Fenniae* 1966; 12: 13-9.
- <sup>4</sup>Dingle JH, Badger CF, Jordan WS. *Illness in the home*. Cleveland: The Press of Western Reserve University, 1964.
- <sup>5</sup>Leeder SR, Corkhill R, Irwig CM, Holland WW, Colley JRT. Influence of family factors on the incidence of lower respiratory illness during the first year of life. *Br J Prev Soc Med* 1976; 30: 203-12.
- <sup>6</sup>Gardner PS. Virus infections and respiratory disease of childhood. *Arch Dis Child* 1968; 43: 629-45.
- <sup>7</sup>Taber LH. Infection with influenza A/Victoria virus in Houston families, 1976. *J Hyg* 1981; 86: 303-13.
- <sup>8</sup>Frank AL, Taber LH, Wells JM. Individuals infected with two subtypes of influenza A virus in the same season. *J Infect Dis* 1983; 147: 120-4.
- <sup>9</sup>Frank AL, Taber LH, Glezen WP, Kasel GL, Wells CR, Paredes A. Breast-feeding and respiratory virus infection. *Pediatrics* 1982; 70: 239-45.
- <sup>10</sup>Baxter BD, Couch RB, Greenberg SB, *et al*. Maintenance of viability and comparison of identification methods for influenza and respiratory viruses of humans. *J Clin Microbiol* 1977; 6: 19-22.
- <sup>11</sup>Frank AL, Couch RB, Griffiths CA, *et al*. Comparison of different tissue cultures for isolation and quantitation of influenza and parainfluenza viruses. *J Clin Microbiol* 1979; 10: 32-6.
- <sup>12</sup>Dowdle WA, Kendal AP, Noble G. Influenza viruses. In: Lennette EH, and Schmidt NJ, eds. *Diagnostic procedures for viral, rickettsial and chlamydial infections*. Washington, DC: American Public Health Association, 1979: 585-609.
- <sup>13</sup>Glezen WP, Paredes A, Allison JE, *et al*. Risk of respiratory syncytial virus infection for infants from low income families in relationship to age, sex, ethnic group and maternal antibody level. *J Pediatr* 1981; 98: 708-15.
- <sup>14</sup>Frank AL, Puck J, Hughes BJ, Cate TR. Microneutralization test for influenza A and B and parainfluenza 1 and 2 viruses that uses continuous cell lines and fresh serum enhancement. *J Clin Microbiol* 1980; 12: 426-32.
- <sup>15</sup>Chanock RM, Parrot RH. Acute respiratory disease in infancy and childhood: present understanding and prospects for prevention. *Pediatrics* 1965; 36: 21-39.
- <sup>16</sup>Murphy TF, Henderson FW, Clyde WA Jr, Collier AM, Denney FW. Pneumonia: an eleven-year study in a pediatric practice. *Am J Epidemiol* 1981; 113: 12-21.
- <sup>17</sup>Parrot RH, Kim HW, Arrobie DS, *et al*. Epidemiology of respiratory syncytial virus infection in Washington, DC. II. Infection and disease with respect to age immunologic status, race and sex. *Am J Epidemiol* 1973; 98: 289-300.

2023379708A

### Discussion

In this study we closely monitored infants for viral infections and respiratory symptoms through the first year of life for five consecutive years. Since we studied proved viral infection regardless of illness and all illnesses regardless of severity, differences in groups based on family recognition of illness and patterns of medical care were minimised. It might therefore be expected that for such a ubiquitous group of viruses and such common illnesses the impact of family and social factors would not be impressive. In fact, we were unable to find any consistent overall relationship between respiratory viral infection or illness and the social factors studied. We had previously noted a similar lack of overall effect of breast feeding on viral respiratory infection and illness in this same population.<sup>10</sup> Within this general similarity of experience among infants living under different conditions, however, there were selected findings of interest, especially in relation to previous reports. This group of observations will be summarised and then discussed individually. RSV and para 3 notably could not be confidently related to any of the study factors. The infection rates of rhino, influenza, and adenoviruses were all significantly associated with two of the study factors but the strongest and clearest relationships were found for influenza viruses. Respiratory illness varied significantly with the study factors only when looking at more serious illness categories. Important trends included variation in severe illness rates with sex and number of siblings while significant relationships existed between LRD, socioeconomic class, and daycare. No differences in LRD were found in relation to parental smoking as an isolated factor.

RSV is a major cause of respiratory illness in young children, especially bronchiolitis and pneumonia.<sup>11-13</sup> Previous studies have found no correlation between RSV infection and sex, race, or socioeconomic class<sup>14-16</sup> although sex, low socioeconomic class, and number of siblings, may influence the outcome of infection.<sup>17-19</sup> Our data also show no correlation between RSV infection and sex, race, or socioeconomic class, and, in addition, we found no association with daycare. The relationship to parental smoking must be considered questionable because of the limitations of the data relative to this virus in 1975-6. Hall *et al* also found a questionable relationship between parental smoking and RSV infection so that any association continues to be undocumented.<sup>20</sup> Sixty nine per cent of our study infants had had at least one RSV infection; this shows the high incidence in this age group.

Parainfluenza type 3 virus is also a major cause of LTB in young children and is an important cause of

bronchiolitis and pneumonia in infants and children,<sup>21</sup> but the influence of social and family factors have been little studied. Our results show a higher incidence of initial infections among infants of low socioeconomic class but no significant association with any of the factors studied. Fifty five per cent of the infants had had at least one parainfluenza 3 virus infection.

Our study indicates that for influenza viruses (particularly type A) both race and number of siblings influence the rate of infection. Kim *et al* found that a larger percentage of black infants (especially boys) in hospital for respiratory illness during 11 influenza epidemics had influenza A virus infection,<sup>22</sup> and our very different approach also gave indications that blacks are at a greater risk for influenza A infection. The effect of race on influenza infection was not influenced by family size or socioeconomic class even though a larger number of non-whites were in the low socioeconomic class. The present data also point to older siblings, particularly school age children, as introducers; infants were more likely to be infected if they had school aged siblings in the home. This was especially true during the epidemic of 1975-6 as previously reported<sup>9</sup> and has been observed by others.<sup>23</sup> Hall *et al* found that preschoolers were more often responsible for spread of infection within the family based on age-specific infection rates, but they noted that infection rates based on a fourfold serological rise rather than the twofold rise they used would have shifted the highest age-specific infection rates to school age children.<sup>24</sup>

Rhinovirus infection rates were found to be influenced by sex and daycare attendance. In both instances the reason appeared to be a high rate of infection in girls attending daycare for which we have no explanation.

Variation in illness with social and family factors was generally restricted to LRD rates and most of the findings reported previously also refer to LRD. Boys have been shown to have higher rates of LRD compared with girls<sup>25-27</sup> at least to the age of 6. Although we found that the difference between boys and girls was not significant for LRD, the ratio of illness, especially when looking only at non-daycare attenders, was very close to the 60:40 ratio found by Gardner.<sup>4</sup> The presence of siblings has also been shown by previous studies to affect the seriousness and number of illnesses.<sup>28-30</sup> We were unable to show that the difference in illness rates between number of siblings was significant for LRD but the trend was very suggestive.

Low socioeconomic status has been thought to influence the rate of respiratory illness by means of overcrowding, large family size, and inadequate medical care.<sup>31</sup> We provided uniform medical care

2023379708

- <sup>10</sup> Glezen WP, Denny FW. Epidemiology of acute lower respiratory disease in children. *N Engl J Med* 1973; 288: 498-504.
- <sup>11</sup> Orstavik I, Carlsen KH, Halvorsen K. Respiratory syncytial virus infections in Oslo 1972-1978. I. Virological and epidemiologic studies. *Acta Paediatr Scand* 1978; 69: 717-22.
- <sup>12</sup> Clarke SKR, Gardner PS, Poole PM, Simpson H, Tobin JO. Respiratory syncytial virus infection. Admissions to hospitals in industrial, urban, and rural areas. *Br Med J* 1978; ii: 796-8.
- <sup>13</sup> Sims OG, Downham MAPS, McQuillin J, Gardner PS. Respiratory syncytial virus infection in north-east England. *Br Med J* 1978; ii: 1095-8.
- <sup>14</sup> Hall CB, Geiman JM, Biggar RB, Rotok DJ, Hogan DM, Douglas RG. Respiratory syncytial virus infections within families. *N Engl J Med* 1976; 294: 414-9.
- <sup>15</sup> Kim HW, Brandt CD, Aronso JO, Murphy B, Chanock RM, Parrot RH. Influenza A and B virus infection in infants and young children during the years 1957-76. *Am J Epidemiol* 1979; 109: 464-79.
- <sup>16</sup> Jordan WS Jr. The mechanism of spread of Asian influenza. *Am Rev Respir Dis* 1961; 83: 29-38.
- <sup>17</sup> Hall CE, Cooney MK, Fox JP. The Seattle virus watch. IV. Comparative epidemiologic observations of infections with influenza A and B viruses 1965-1969 in families with young children. *Am J Epidemiol* 1973; 98: 365-80.
- <sup>18</sup> Colley JRT. The vulnerable child. *J R Coll Gen Pract* 1975; 25: 257-62.
- <sup>19</sup> Strangert K. Respiratory illness in preschool children with different forms of daycare. *Pediatrics* 1976; 57: 191-6.
- <sup>20</sup> Loda FA, Glezen WP, Clyde WA Jr. Respiratory disease in group day care. *Pediatrics* 1972; 49: 428-37.
- <sup>21</sup> Vihma L. Surveillance of acute viral respiratory disease in children. *Acta Paediatr Scand* 1969; 192, suppl: 1-52.
- <sup>22</sup> Harlap S, Davies AM. Infant admissions to hospital and maternal smoking. *Lancet* 1974; i: 329-32.

2023379709



Harrington, W., Krupnick, A.J. "Short-Term Nitrogen Dioxide Exposure and Acute Respiratory Disease in Children" J Air Pollut Control Assoc 35: 1061-1067, 1985.

ABSTRACT. A CHES data base from Chattanooga, Tennessee was thoroughly scrutinized and found to be of high enough quality to warrant epidemiological analysis. Using this data base, the relationship between NO<sub>2</sub> ambient pollution levels and acute respiratory disease in children was examined. Although a statistically significant relationship was found, it was not monotonic. Indeed, over the range of pollution values experienced, more illness is associated with low pollution values than with high ones. A U-shaped relationship between illness and NO<sub>2</sub> concentrations was found in several subpopulations in addition to the entire data set, although for some subpopulations no relationship was found. In contrast, higher ambient sulfate levels were found to have a positive effect on acute respiratory disease incidence in children over the entire period and for different subsamples, although this effect was not significant for either season analyzed separately.

2023379711

# Short-Term Nitrogen Dioxide Exposure and Acute Respiratory Disease in Children

Winston Harrington and Alan J. Krupnick  
Resources For The Future  
Washington, D.C.

A CHES data base from Chattanooga, Tennessee was thoroughly scrutinized and found to be of high enough quality to warrant epidemiological analysis. Using this data base, the relationship between  $\text{NO}_2$  ambient pollution levels and acute respiratory disease in children was examined. Although a statistically significant relationship was found, it was not monotonic. Indeed, over the range of pollution values experienced, more illness is associated with low pollution values than with high ones. A U-shaped relationship between illness and  $\text{NO}_2$  concentrations was found in several subpopulations in addition to the entire data set, although for some subpopulations no relationship was found. In contrast, higher ambient sulfate levels were found to have a positive effect on acute respiratory disease incidence in children over the entire period and for different subsamples, although this effect was not significant for either season analyzed separately.

Since the passage of the Clean Air Act in 1970, several epidemiological studies have attempted to associate morbidity with indoor and outdoor exposure to nitrogen dioxide ( $\text{NO}_2$ ). The indoor, so-called gas stove studies<sup>1-7</sup> produced mixed and inconclusive results in their attempts to link health impairment to the presence of a gas stove or gas heater in the home. Studies of the health effects of outdoor  $\text{NO}_2$  exposures also have failed to find consistently significant health effects at ambient exposure levels.<sup>8-11</sup>

In an analysis of people living in Chattanooga, Tennessee, conducted under the Community Health and Environmental Surveillance System (CHES) program, Shy and Love<sup>12</sup> were able to link  $\text{NO}_2$  exposures and acute respiratory disease. However, several problems have been raised about this study. The researchers have been criticized for using rudimentary statistical techniques, consisting mainly of pairwise comparison of illness incidence rates in subpopulations. In addition, the data base has been tainted by its association with the controversial CHES program.<sup>13</sup> [The earlier CHES Chattanooga studies were also criticized for using a subsequently discredited method (Jacobs-Hochheiser) for monitoring  $\text{NO}_2$  concentrations. However, by 1972 the Saltzman technique was being used.] Yet EPA has found the Chattanooga data to be accurately transferred from the surveys to the computer tapes and our own research has revealed the data quality to be at least as high as other similar, but much less controversial data bases.

The lack of persuasive epidemiological studies upon which to base a national ambient air quality standard for nitrogen dioxide motivated the present paper. Here we return to the CHES aerometric and health data bases collected during

1972-73 in Chattanooga and used by Shy and Love to examine the relationship between  $\text{NO}_2$  and acute respiratory disease in children. We first describe and defend the CHES-Chattanooga data base and the statistical model used to examine it. We then present our results and discuss a number of econometric issues and their relationship to our findings.

## The Data Base

In January 1972, a self-administered survey on chronic respiratory disease (CRD) was distributed to families with children in elementary schools in one of the three Chattanooga communities, Harrison, Brainerd, and Redbank, located within one mile of an air pollution monitoring station. A subsample of families—1970 parents and their children, 4898 individuals in all—was drawn from this sample to participate in an acute respiratory disease (ARD) panel survey. Information was taken in two-week intervals (always beginning on a Sunday) over three school semesters from spring 1972 through spring 1973. Each family was phoned within several days after the end of each two-week period to determine if any family members experienced various acute respiratory disease symptoms or consulted a physician.

Aerometric data were gathered at seven sites. Hourly measurements of  $\text{NO}_2$  were taken using the Saltzman chemiluminescence technique only for the fall 1972 and spring 1973 study periods. Thus, we eliminated data for the spring 1972 period from our analysis. Chattanooga was chosen as a site for an  $\text{NO}_2$  study because it featured a TNT plant emitting large quantities of nitrogen-based pollutants. This plant closed January 1, 1973, resulting in reduced  $\text{NO}_2$  concentrations in the nearby communities. Daily readings were taken on particulates, nitrates, and sulfates. These daily readings were reduced to monthly frequency distributions. Unfortunately, the original daily data were unavailable from EPA, and we have been forced to use the monthly frequency distributions for the latter three pollutants.

The Chattanooga health and aerometric data collection effort of the early 1970s and the CHES program in general have been criticized (Roth<sup>14</sup>) for their poor survey protocols, health data inconsistencies, and aerometric data unreliability. Krupnick and Harrington<sup>15</sup> provide a complete reanalysis of these data and find, first, that the survey protocols were carefully designed and observed. In addition, responses to identical sociodemographic questions on the CRD and ARD surveys were found to be quite consistent. Also, the  $\text{NO}_2$  monitoring data were found to be reasonably complete, generally consistent, and taken by devices that generally outperform other types of monitors in the lab.

Further, because a duplicate CRD survey was administered to some of the participants 22 months later, we were

Copyright 1985-Air Pollution Control Association



able to identify inconsistencies intertemporally. Drawing on responses from 948 parents and considering only the questions concerning age, race, birthdate, education, and smoking status, over 80% of the parents had matching responses over the two surveys. These results compare favorably to similar investigations of the U.S. Census and other highly regarded data bases.<sup>14,17</sup>

In the course of our examination of the quality of this data base we noted a number of recall-related problems inherent in the survey procedure. These problems may also be present in parts of other surveys, such as the Health Interview Survey (HIS), that rely on biweekly interviews to collect acute respiratory disease data. These problems are discussed in some detail elsewhere,<sup>18</sup> but the main points may be summarized as follows:

1) Respondents have imperfect recall of the day or even week of onset of illness. For example, over 60% of illnesses reported were said to have occurred in the second week of the recall period, a result significantly ( $\alpha = 0.01$ ) different from the uniform distribution one would expect. Apparently respondents either forget (presumably minor) illnesses occurring in the first week, or they remember disease onset as occurring later than was actually the case.

2) When average duration of reported illness is plotted as a function of day of onset during the two-week period, a linear decline is found during the second week of the period, with average duration at the end of the week barely half of average duration at the beginning. The most likely explanation is that illnesses extending past the end of the period are not reported accurately, even though interviewers were instructed to identify such illnesses and ask about them at the end of the next reporting period. If this explanation is correct, the truncation of restricted activity days imparts a downward bias to illness severity.

3) In other panel studies it has been suggested that respondents may, over time, progressively under-report illness simply because they become tired of doing interviews. If pollution levels are time-dependent, the study results may be biased accordingly. We found little evidence of this phenomenon. On the assumption that less serious illnesses could

Table II. Pollution statistics.

	Mean ( $\mu\text{g}/\text{m}^3$ )	Standard deviation	Correlation coefficients		
			PAR90P	SUL90P	TEMP
NO2MAX	98.0	48.3	-0.10	0.20	-0.09
PAR90P	100.6	31.4		-0.027	0.34
SUL90P	10.0	2.7			-0.036

be more likely to be neglected, we regressed the ratio of "serious" to total illness incidence on time, and found no trend.

These findings affected our subsequent data analysis in two ways. First, no attempt was made to use time intervals shorter than two weeks, even though the sample could be reduced to weekly or even daily observations. Second, we concentrated on the incidence of illness rather than duration, inasmuch as we felt the former to be more reliable.

### The Model

To identify the factors affecting reported children's disease, we use pooled cross-section time series models predicting illness incidence or duration as a function of demographic, pollution, and weather variables. Symbolically, the models are of the form

$$S_{ijt} = f(X_{ij}, P_{jt}, W_t) + \epsilon_{ijt}$$

where  $S_{ijt}$  is the reported incidence or duration of the illness of the  $i$ th child in the  $j$ th neighborhood during period  $t$ ,

$X_{ij}$  is a vector of personal variables for the  $i$ th child in the  $j$ th neighborhood,

$P_{jt}$  is a vector of pollution variables for the  $j$ th neighborhood in period  $t$ ,

$W_t$  is the weather in period  $t$ , and

$\epsilon_{ijt}$  is the disturbance term.

The independent variables are defined as follows:

AGE:	the child's age at the beginning of the school year.
RACE1W:	the race of the head of household; 1 if white, 0 if nonwhite.
CHESTINF:	1 if the child has suffered a respiratory infection within the past three years, 0 otherwise.
CHRON:	1 if the child suffers from asthma or a chronic heart or lung condition, 0 otherwise.
EDU:	the years of schooling completed by the head of household.
MOMHEAD:	1 if the household head is female, 0 otherwise.
SMKPPD:	mother's smoking in packs per day.
CROWD:	number of household members divided by the number of rooms in the house.
SEX1F:	sex of child; 1 if female, 0 if male.
GAS:	1 if the kitchen stove is gas, 0 if electric.
RAIN:	amount of rainfall during the period, in inches.
EPIDEM:	monthly influenza cases reported by the State of Tennessee (in thousands).
TEMP:	the absolute difference between the average temperature during the period and 65°.
NO2MAX:	average daily maximum concentration of $\text{NO}_2$ , in $\mu\text{g}/\text{m}^3$ .
PAR90P:	90th percentile total suspended particulate concentration during the month, in $\mu\text{g}/\text{m}^3$ .
SUL90P:	90th percentile sulfate concentration during the month, in $\mu\text{g}/\text{m}^3$ .

As noted above, two dependent variables are considered: illness incidence (NEWILL), which is 0 or 1 according to

Table I. Descriptive statistics ( $N = 2093$ ).

Variable	Mean value or population fraction
NEWILL	0.13
RADS	0.21
AGE	7.7
Age distribution	
0-2	0.09
3-4	0.08
5-6	0.16
7-8	0.23
9-10	0.25
11-12	0.19
RACE1W	0.91
CHESTINF	0.28
CHRON	0.07
Education of household head	
High school graduate	0.71
Attended some college	0.45
MOMHEAD	0.05
Mothers' smoking status	
Current	0.32
Ex-	0.15
Non-	0.53
CROWD	1.30
SEX1F	0.48
GAS	0.05
RAIN	2.70
TEMP	18.20

Table III. Predicting illness incidence in population subsamples<sup>a</sup>

	A	B	C	D	E	F	G	H	I
	All children 12 and under	Children with nonsmoking mothers	Children with smoking mothers	Children without chronic respiratory disease	Children with CRD	Children 6 and under	Infants	Fall only	Spring only
Intercept	0.0512 (0.0503)	0.084 (0.059)	-0.0197 (0.091)	0.052 (0.056)	0.098 (0.095)	0.037 (0.10)	0.151 (0.21)	0.161 (0.113)	0.018 (0.075)
NO2MAXL	-8.87E-4 (2.05E-4) <sup>c</sup>	-6.10E-4 (2.46E-4) <sup>b</sup>	-13.5E-4 (3.71E-4) <sup>c</sup>	-6.4E-4 (2.3E-4) <sup>c</sup>	-13.6E-4 (4.0E-4) <sup>c</sup>	-8.44E-4 (4.1E-4) <sup>b</sup>	-12.5E-4 (8.7E-4)	0.26E-4 (4.3E-4)	-15.0E-4 (2.9E-4) <sup>c</sup>
NO2MAXH	1.71E-4 (0.68E-4) <sup>b</sup>	2.19E-4 (0.78E-4) <sup>b</sup>	-5.7E-4 (1.46E-4)	2.3E-4 (1.13E-4) <sup>b</sup>	5.1E-4 (1.34E-4)	2.41E-4 (1.89E-4)	5.2E-4 (2.55E-4) <sup>b</sup>	0.06E-4 (0.78E-4)	3.95E-4 (2.01E-4) <sup>b</sup>
PAR90P	8.88E-4 (6.08E-4)	6.69E-4 (7.4E-4)	14.3E-4 (10.8E-4)	11.4E-4 (6.8E-4)	4.00E-4 (12E-4)	12.1E-4 (11.9E-4)	13.0E-4 (24E-4)	28.1E-4 (15E-4)	13.4E-4 (8.1E-4)
PAR90P2	-0.053E-4 (0.026E-4) <sup>c</sup>	-0.044E-4 (0.03E-4)	-0.075E-4 (0.048E-4)	-0.058E-4 (0.031E-4)	-0.041E-4 (0.0555)	-0.066E-4 (0.054)	0.045E-4 (0.11E-4)	-0.146E-4 (0.074E-4)	-0.056E-4 (0.039E-4)
SUL90P	135E-4 (45.9E-4) <sup>c</sup>	117E-4 (54E-4) <sup>b</sup>	191E-4 (87E-4) <sup>b</sup>	89.8E-4 (53E-4)	231E-4 (87.8E-4) <sup>c</sup>	128E-4 (90E-4)	219E-4 (195E-4)	-156E-4 (217E-4)	95.3E-4 (65.7E-4)
SUL90P2	-5.54E-4 (1.72E-4) <sup>c</sup>	-4.81E-4 (2.0E-4) <sup>b</sup>	-7.91E-4 (3.32E-4) <sup>b</sup>	-3.67E-4 (1.97E-4)	-9.36E-4 (3.24E-4)	-5.46E-4 (3.3E-4)	-11.6E-4 (7.5E-4)	5.76E-4 (9.9E-4)	-3.38E-4 (2.2E-4)
AGE	-0.0185 (0.0034) <sup>c</sup>	-0.0165 (0.0042) <sup>c</sup>	-0.0252 (0.0057) <sup>c</sup>	-0.022 (0.0037) <sup>c</sup>	-0.010 (0.0071)	d	e	-0.0207 (0.0047) <sup>c</sup>	-0.0164 (0.0048) <sup>c</sup>
AGE2	7.53E-4 (2.44E-4) <sup>c</sup>	5.14E-4 (3.0E-4)	14.9E-4 (4.2E-4) <sup>c</sup>	8.99E-4 (2.66E-4) <sup>c</sup>	3.32E-4 (5.27E-4)	d	e	8.71E-4 (3.47E-4) <sup>c</sup>	6.4E-4 (3.46E-4)
CHESTINF	0.0475 (0.010) <sup>c</sup>	0.0495 (0.012) <sup>c</sup>	0.044 (0.018) <sup>c</sup>	0.044 (0.011) <sup>c</sup>		0.071 (0.019) <sup>c</sup>	0.103 (0.042) <sup>b</sup>	0.046 (0.014) <sup>c</sup>	0.048 (0.015) <sup>c</sup>
CHRON	0.044 (0.0059) <sup>c</sup>	0.0390 (0.0071) <sup>c</sup>	0.052 (0.011) <sup>c</sup>			0.036 (0.011) <sup>c</sup>	0.003 (0.024)	0.036 (0.0083) <sup>c</sup>	0.052 (0.0084) <sup>c</sup>
CROWD	0.0184 (0.0073) <sup>b</sup>	0.0163 (0.0090)	0.018 (0.013)	0.019 (0.0083) <sup>b</sup>	0.011 (0.014)	0.037 (0.017) <sup>b</sup>	0.029 (0.715)	0.022 (0.010) <sup>b</sup>	0.0156 (0.010)
EDU	-0.0012 (0.0021)	-0.0045 (0.0028)	0.0056 (0.0039)	-0.0016 (0.0025)	-0.0060 (0.0095)	-0.0029 (0.0046)	-0.0031 (-0.315)	-0.00028 (0.0031)	-0.0024 (0.0032)
EPIDEM	0.072 (0.011) <sup>c</sup>	0.089 (0.013) <sup>c</sup>	0.036 (0.019)	0.055 (0.012) <sup>c</sup>	0.099 (0.021) <sup>c</sup>	0.064 (0.022) <sup>c</sup>	0.059 (1.31)	-0.23 (0.085) <sup>c</sup>	0.098 (0.017) <sup>c</sup>
SEX1F	0.0076 (0.0052)	0.0083 (0.0063)	0.006 (0.0092)	0.0066 (0.0058)	0.011 (0.010)	-0.0080 (0.011)	0.0027 (0.023)	0.0021 (0.0072)	0.012 (0.0071)
SMKPPD	-0.0013 (0.0020)		0.0019 (0.0049)	-0.0027 (0.0023)	0.0021 (0.0036)	-0.0050 (0.0040)	-0.0058 (0.0086)	0.00126 (0.0028)	-0.0037 (0.0028)
GAS	-0.020 (0.012)	-0.044 (0.015) <sup>c</sup>	0.012 (0.019)	0.0044 (0.014)	-0.061 (0.021) <sup>c</sup>	-0.057 (0.026) <sup>b</sup>	-0.070 (0.061)	-0.0012 (0.016)	-0.036 (0.016) <sup>b</sup>
RAIN	-0.0056 (0.0016) <sup>c</sup>	-0.0068 (0.0019) <sup>c</sup>	-0.0027 (0.0027)	-0.0050 (0.0017) <sup>c</sup>	-0.0060 (0.0031)	-0.0054 (0.0032)	0.0019 (0.0064)	-0.019 (0.0053) <sup>c</sup>	-0.0027 (0.0020)
TEMP	0.0022 (0.00041) <sup>b</sup>	0.0021 (0.00048) <sup>c</sup>	0.0025 (0.00072) <sup>c</sup>	0.0020 (0.00045) <sup>c</sup>	0.0026 (0.00081) <sup>c</sup>	0.0029 (0.00082) <sup>c</sup>	0.0015 (0.0018)	0.0018 (0.00086) <sup>b</sup>	0.0026 (0.00066) <sup>c</sup>
RACE1W	0.056 (0.0090) <sup>c</sup>	0.039 (0.012) <sup>c</sup>	0.073 (0.14) <sup>c</sup>	0.051 (0.0095) <sup>c</sup>	0.060 (0.019) <sup>c</sup>	0.059 (0.017) <sup>c</sup>	0.087 (0.039) <sup>b</sup>	0.034 (0.013) <sup>c</sup>	0.075 (0.013) <sup>c</sup>
N	16474	11497	4977	11557	5246	5108	1387	8176	8298
F	25.5	19.7	8.83	15.29	8.33	5.68	1.84	8.37	22.5
R <sup>2</sup>	0.0286	0.030	0.033	0.022	0.026	0.027	0.025	0.019	0.049

<sup>a</sup> Standard errors in parentheses.<sup>b</sup> Significant at the 5% level.<sup>c</sup> Significant at the 1% level.<sup>d</sup> AGE and AGE2 were replaced by dummy variables AGEONE (= 1 if AGE = 1, 0 otherwise) and AGETWO.<sup>e</sup> AGE and AGE2 were replaced by dummy variables AGEONE through AGESIX.

whether the child is reported ill during the two-week period in question, and duration of restricted activity (RADS), which takes an integer value between 0 and 14.

Tables I and II provide descriptive statistics on these variables. Note the low number for mean RADS, indicating the large percentage of observations with a zero value for this variable. Correlation coefficients between each of the pollutants and temperature are also provided. Note that correlations between pollutants are all quite low. We searched for more complicated patterns of collinearity by using the diagnostic tests<sup>18</sup> provided with the SAS regression package. These tests failed to reveal any serious collinearity problems involving any of the independent variables.

We relied primarily on a linear probability model for our analysis, using ordinary least squares (OLS) as the estimation procedure, the results of which are presented below. However, the OLS model requires a number of assumptions of questionable validity for the current problem. We discuss later the effects of these assumptions on the outcomes.

## Results

Table III shows the results of the regressions predicting illness incidence. Column A gives the results for the entire sample of children aged 12 and under. The remaining columns show results for a number of subpopulations; we used these results to examine the stability of the coefficients and to identify populations especially sensitive to the pollution variables. Thus, Columns B and C give results for children of mothers who do and do not smoke, and Columns D and E give results for children with and without chronic respiratory disease or a history of respiratory ailments. In Columns F and G we examine the illness incidence in younger children. Finally, in Columns H and I we divide the sample into fall (October–December 1972) and spring (January–April 1973) time periods.

The specification of the NO<sub>2</sub> variable was piecewise linear, with a break at 100 µg/m<sup>3</sup>. This specification was the best of all those examined. In Table III NO2MAXL and NO-

2023379714

2MAXH refer, respectively, to average daily maximum concentrations below and above  $100 \mu\text{g}/\text{m}^3$ . As shown, for NO-2MAX concentrations below  $100 \mu\text{g}/\text{m}^3$ , illness probability falls relatively sharply as NO2MAX increases. Above  $100 \mu\text{g}/\text{m}^3$ , illness probability gradually increases with NO-2MAX, but the illness rate at the highest observed two-week maximum concentration ( $384 \mu\text{g}/\text{m}^3$ ) is less than that at the lowest observed concentration ( $27 \mu\text{g}/\text{m}^3$ ). The clinical literature gives no reason why a dose-response function should have these characteristics.

In the subsamples (Columns B to I), the above relationship between NO2MAX and illness is replicated for children with nonsmoking mothers and children without a history of respiratory disease. For both preschool age children and infants, the coefficients were similar although not always significant. However, for children whose mothers smoke or have a chronic respiratory condition, NO2MAXH has virtually no effect. Finally, when only fall periods are examined, NO2MAX is not related to illness at all.

These exceptions did not increase our confidence in the results. The first two exceptions suggest that a "sensitive population" for NO<sub>2</sub> is healthy older children of nonsmoking mothers. If so, perhaps the presence of a chronic condition swamps the small NO<sub>2</sub> effect. Likewise, perhaps for children exposed to parental smoking an additional NO<sub>2</sub> effect cannot be detected. One problem with this explanation is that we found no adverse effect of mother's smoking on children's health. As for the absence of an NO<sub>2</sub> effect in the fall, we note that the prevalence of illness in that season was relatively low in any event. If the effect of NO<sub>2</sub> is to reduce resistance to disease, we might expect to find no NO<sub>2</sub> effect when little disease is present in the community. Such speculation notwithstanding, we have not found an effect from NO<sub>2</sub> that is supported by clinical evidence or that is present in all population subgroups.

For sulfates and particulates the best fits were obtained for the 90th percentile of two-week concentration and a quadratic specification, with a positive linear and negative square term. The particulate results were reasonably consis-

tent across subpopulations, but rarely significant at the 5% level. Moreover, the various functions were such that the effects of particulates on illness were negative at concentrations below  $80\text{--}100 \mu\text{g}/\text{m}^3$ , which is near the average 90th percentile concentration. That is, over much of the relevant range the particulate variable is inversely related to illness.

The coefficients for sulfates are significant for the entire sample, but not for the fall and spring semesters separately. For fall, the coefficients enter with signs and reverse of all other subsamples, but the *t*-values are very small. For spring, the coefficients are similar to coefficients in other equations but the *t*-values still are not significant. For the population subsamples the sulfate coefficients are stable and significant except for infants, where, as we have noted, sample sizes are much smaller and an effect of population on health would be correspondingly more difficult to identify. The inconsistent seasonal results may be related to using weighted averages of monthly summaries of daily readings instead of two-week averages, which were unavailable for particulates and sulfates.

Turning briefly to the other explanatory variables, the most statistically significant and robust results were for variables that one would expect to be associated with respiratory disease: age, a history of chest infection, presence of a chronic condition, the extent of crowding in the home, and outside temperature. Not only were these variables almost always significant, but the coefficients were stable across subpopulations. The coefficients for CHRON (presence of chronic disease), for example, varied between 0.036 and 0.052, except in the equation for infants, and indeed very few infants in the sample were diagnosed for a chronic disease. The EPIDEM variable was also generally significant but in the fall the sign was negative, a result we believe to be fortuitous, inasmuch as the variable was very small in absolute value during that season.

For two other variables, RACE1W and RAIN, the results were stable and significant. White children consistently reported more new illness than nonwhites. We also found a consistent inverse relationship between the amount of rain-

Table IV. Comparison of specifications of NO<sub>2</sub> variables in equations predicting illness incidence.<sup>a</sup>

	A	B	C	D	E	F	G
NO2MAX	1.4E-6 (56.8E-6)	-3.5E-4 (1.82E-4) <sup>b</sup>	-21.7E-4 (4.37E-4) <sup>c</sup>				
NO2MAX2		0.009E-4 (0.0045E-4)	11.3E-6 (2.31E-6) <sup>c</sup>				
NO2MAX3			-1.59E-8 (0.35E-8) <sup>c</sup>				
NO2MAX(0-75)				-19E-4 (4.63E-4) <sup>c</sup>	-21E-4 (4.88E-4) <sup>c</sup>		
NO2MAX(75-150)				-0.16E-4 (0.94E-4)			
NO2MAX(75-100)					-0.28E-4 (0.80E-4)		
NO2MAX(100-150)					1.2E-4 (1.1E-4)		
NO2MAX(>150)				1.7E-4 (1.15E-4)	0.56E-4 (1.19E-4)		
NO2MAX(0-100)						-8.9E-4 (2.05E-4) <sup>c</sup>	
NO2MAX(>100)						1.7E-4 (0.69E-4) <sup>b</sup>	
NO2AVG(0-50)							-9.4E-4 (4.1E-4) <sup>b</sup>
NO2AVG(>50)							1.96E-4 (3.8E-4) <sup>b</sup>
F	25.8	24.7	24.5	24.0	23.2	25.5	24.7
R <sup>2</sup>	0.0274	0.0277	0.0289	0.0281	0.0288	0.0286	0.0278
N	16474	16474	16474	16474	16474	16474	16474

<sup>a</sup> Standard errors in parentheses.

<sup>b</sup> Significant at the 5% level.

<sup>c</sup> Significant at the 1% level.

Table V. Cross section time series regression coefficients for illness incidence and restricted activity days: full sample vs. sample consisting of one child per family.<sup>a</sup>

Variable	Illness incidence		Restricted activity days	
	Full sample	Sub-sample	Full sample	Sub-sample
Intercept	0.0512 (0.06)	-0.0016 (0.73)	0.348 (0.135) <sup>b</sup>	0.275 (0.20)
NO2MAXL	-8.87E-4 (2.05E-4) <sup>c</sup>	-7.98E-4 (2.9E-4) <sup>c</sup>	-25.0E-4 (5.6E-4) <sup>c</sup>	-28.7E-4 (8.3E-4) <sup>c</sup>
NO2MAXH	1.71E-4 (0.68E-4) <sup>b</sup>	1.39E-4 (0.99E-4)	4.4E-4 (1.86E-4) <sup>b</sup>	6.22E-4 (2.8E-4) <sup>b</sup>
PAR90P	8.88E-4 (6.08E-4)	17.8E-4 (8.8E-4) <sup>b</sup>	-18.3E-4 (16.6E-4)	9.80E-4 (24.5E-4)
PAR90P2	-0.053E-4 (0.028E-4)	-0.088E-4 (0.040E-4) <sup>b</sup>	0.064E-4 (0.075E-4)	-0.04E-4 (0.099)
SUL90P	135E-4 (45.9E-4) <sup>c</sup>	107E-4 (66E-4)	212E-4 (126E-4)	73.3E-4 (185E-4)
SUL90P2	-5.54E-4 (1.72E-4) <sup>c</sup>	-4.73E-4 (2.5E-4)	-9.3E-4 (4.7E-4) <sup>b</sup>	-4.26E-4 (6.9E-4)
AGE	-0.0185 (0.0034) <sup>c</sup>	-0.020 (0.0049) <sup>c</sup>	-0.045 (0.0092) <sup>c</sup>	-0.044 (0.014) <sup>c</sup>
AGE <sup>2</sup>	7.53E-4 (2.44E-4) <sup>c</sup>	8.54E-4 (3.6E-4) <sup>b</sup>	20.9E-4 (6.7E-4) <sup>c</sup>	19.1E-4 (10.0E-4)
CHESTINF	0.0475 (0.010) <sup>c</sup>	0.053 (0.015) <sup>c</sup>	0.178 (0.028) <sup>c</sup>	0.196 (0.042) <sup>c</sup>
CHRON	0.044 (0.0059) <sup>c</sup>	0.047 (0.0084) <sup>c</sup>	0.099 (0.016) <sup>c</sup>	0.110 (0.023) <sup>c</sup>
CROWD	0.0184 (0.0073) <sup>b</sup>	0.018 (0.010)	0.019 (0.020)	0.080 (0.026)
EDU	-0.0012 (0.0021)	0.0028 (0.0032)	-0.0087 (0.0061)	-0.0023 (0.0088)
EPIDEM	0.072 (0.011) <sup>c</sup>	0.080 (0.015) <sup>c</sup>	0.228 (0.029) <sup>c</sup>	0.221 (0.042) <sup>c</sup>
SMKPPD	-0.0013 (0.0020)	-0.0039 (0.0028)	0.0004 (0.0050)	0.0086 (0.0078)
GAS	-0.020 (0.012)	-0.0021 (0.0016)	-0.037 (0.032)	0.0021 (0.045)
RAIN	-0.0056 (0.0016) <sup>c</sup>	-0.0049 (0.0022) <sup>b</sup>	-0.0037 (0.0043)	0.0025 (0.0061)
TEMP	0.0022 (0.0004) <sup>c</sup>	0.0020 (0.00057) <sup>c</sup>	0.0029 (0.0011) <sup>c</sup>	0.0030 (0.0016)
RACE1W	0.056 (0.0090) <sup>c</sup>	0.065 (0.014) <sup>c</sup>	0.127 (0.025) <sup>c</sup>	0.136 (0.038) <sup>c</sup>
SEX1F	0.0076 (0.0052)	0.0094 (0.0074)	0.023 (0.014)	-0.0039 (0.021)
N	16474	8158	16474	8158
F	25.5	13.6	20.5	10.6
R <sup>2</sup>	0.0286	0.031	0.023	0.024

<sup>a</sup> Standard errors in parentheses.

<sup>b</sup> Significant at the 5% level.

<sup>c</sup> Significant at the 1% level.

fall and the incidence of illness in a two-week period, although the magnitude varied by a factor of six between fall and spring. Again, we have no explanation for this result. In addition, the presence of a gas stove in the house appeared to be unrelated to disease incidence. Few significant results were obtained, and for those that were significant the sign was contrary to expectation. As only 5% of the households cooked with gas, these generally inconsistent results are not particularly surprising.

Other covariates had virtually no explanatory power, and were rather unstable across subpopulations: educational level of head of household, sex, and mother's smoking status. In particular, we found that a mother's smoking in the home was unrelated to acute respiratory disease incidence of her children. However, this should not be too surprising in view of the contradictory findings on the health effects of passive smoking.<sup>19</sup>

An analysis was also carried out for illness duration as the dependent variable. In this case the dependent variable  $S_{ijt}$  took an integer value between 0 and 14. OLS estimates predicting illness duration were very similar to the results presented above; that is, independent variables that were

also significant and significant. However, OLS estimates of truncated variables are inconsistent as well as inefficient,<sup>20</sup> so it is especially important to compare the results to those of a more suitable estimation procedure. Thus, illness duration was also investigated using Poisson regression, and the comparison between Poisson and OLS is discussed below.

### Some Problems of Estimation

A pervasive problem in the estimation of the effects of air pollution on illness is that information on personal exposure to pollutants is rarely available. Researchers have been obliged to use ambient monitoring data as a proxy for personal exposure, and our study is no exception to this rule. Nonetheless, every child in our sample lived and attended school within a mile of a monitoring site, a relatively tight radius compared to most similar studies.

Besides this measurement difficulty, there were several major econometric problems. These problems arose primarily from our desire to use a linear probability model and OLS as the principal estimation procedure. Convenient though it may be, the OLS model requires a number of assumptions of questionable validity for the current problem. The question we now examine is whether these refinements make much difference to outcomes.

The first problem is that the dependent variable  $S_{ijt}$  is limited to the values 0 or 1 (for illness incidence) or to the small positive integers (for illness duration). Thus, the OLS estimators are not efficient, and the linear probability model may not be appropriate in any event.

A second problem is concerned with the functional form of the relationship between illness and air pollution (indeed, between illness and any explanatory variable). As there is no theory to guide the selection of functional form, we chose a functional form on the basis of an information criterion proposed by Sawa.<sup>21</sup>

The third problem involves the structure of the disturbance term  $\epsilon_{ijt}$ . We examined two alternatives to the OLS assumption of uncorrelated disturbances:

**Autoregression:** an individual's health status in one period may affect his or her health status in subsequent periods, in which case  $E(\epsilon_{ijt}\epsilon_{ijt'}) \neq 0$  for  $t \neq t'$ .

**Contagion:** one's health may be affected by the health of others, especially family members and classmates, in which case  $E(\epsilon_{ijt}\epsilon_{ijt'}) \neq 0$  for  $i \neq i'$  or  $j \neq j'$ .

These problems were examined sequentially. First, several alternative functional forms were examined. Having selected a functional form, we then examined the error structure. Finally, alternative estimation procedures more suited to limited dependent variables were investigated.

### Functional Form

Table IV shows the relationship between illness incidence and NO<sub>2</sub> for several different specifications of the pollution variable. The basic variable was NO2MAX, the daily maximum NO<sub>2</sub> reading, averaged over the two-week period. (Not shown are specifications using average pollution variables, which give results inferior to the ones for NO2MAX.)

The specifications examined include the following:

- linear specification
- quadratic
- cubic
- piecewise linear functions with one break point at 100  $\mu\text{g}/\text{m}^3$ , two break points at 75 and 150  $\mu\text{g}/\text{m}^3$ , and three break points at 75, 100 and 150  $\mu\text{g}/\text{m}^3$ .

In all specifications, except the linear, the relationship between NO<sub>2</sub> and illness incidence is U-shaped. Based on

Table VI. Comparison of logit and OLS models predicting illness incidence.

	OLS		Logit		$\frac{\partial S}{\partial x}$
	Coefficient	Std. error	Coefficient	Std. error	
Intercept	0.176	0.029 <sup>b</sup>	-1.80	0.256	
NO2MAXL	-8.98E-4	2.04E-4 <sup>b</sup>	-0.0067	0.00174 <sup>b</sup>	-7.63E-4 <sup>b</sup>
NO2MAXH	1.61E-4	0.68E-4 <sup>a</sup>	0.00135	0.000595 <sup>a</sup>	1.53E-4 <sup>a</sup>
PAR90P	-2.63E-4	0.923E-4 <sup>a</sup>	-0.00187	0.00082 <sup>b</sup>	-2.13E-4 <sup>a</sup>
SUL90P	2.55E-4	12.1E-4 <sup>a</sup>	-0.00138	0.0108	-1.57E-4
AGE	-0.0082	0.00085 <sup>b</sup>	-0.0715	0.0074 <sup>b</sup>	-0.00814 <sup>b</sup>
CROWD	0.150	0.0071 <sup>a</sup>	0.151	0.064 <sup>a</sup>	0.0172 <sup>a</sup>
EPIDEM	0.074	0.010 <sup>b</sup>	0.537	0.087 <sup>a</sup>	0.061 <sup>b</sup>
GAS	-0.020	0.012	-0.187	0.110	-0.020
RAIN	-0.0063	0.0016 <sup>b</sup>	-0.051	0.015 <sup>b</sup>	-0.0058 <sup>b</sup>
TEMP	0.00184	0.00039 <sup>b</sup>	0.0167	0.00356 <sup>b</sup>	0.00190 <sup>b</sup>
RACE1W	0.0540	0.0088 <sup>b</sup>	0.542	0.093 <sup>b</sup>	0.0528 <sup>b</sup>
CHRON	0.0416	0.0059 <sup>b</sup>	0.350	0.0450 <sup>b</sup>	0.0423 <sup>b</sup>
CHESTINF	0.0460	0.0102 <sup>b</sup>	0.342	0.081 <sup>b</sup>	0.0434 <sup>b</sup>

<sup>a</sup> Significant at the 5% level.<sup>b</sup> Significant at the 1% level.

the BIC criterion proposed by Sawa,<sup>21</sup> the best performer is the piecewise linear specification with a break point at 100  $\mu\text{g}/\text{m}^3$ .

We also tested these spline specifications against the quadratic specification using one of the tests described by Davidson and MacKinnon<sup>22</sup> for non-nested models. The result of this test was as follows: When the quadratic specification was taken as the null hypothesis against the piecewise linear alternative, the null hypothesis was rejected. However, with the spline taken as the null hypothesis the null could not be rejected. Thus, the spline specification with a break point at 100  $\mu\text{g}/\text{m}^3$  fit the data best, and this was used in subsequent work.

#### Error Structure

To examine the effect of possible serial correlation we assumed a first-order autocorrelation scheme and used a two-stage procedure described by Kmenta.<sup>23</sup> First we estimated the autocorrelation parameter  $\rho$  using OLS, and then reestimated the model

$$(Y_t - \hat{\rho} Y_{t-1}) = (X_t - \hat{\rho} X_{t-1})\beta + (\epsilon_t - \hat{\rho} \epsilon_{t-1})$$

Our estimate for  $\rho$  was  $\hat{\rho} = 0.036$ . In the second stage, we found the following results for the NO<sub>2</sub> variables, which, it will be noted, are essentially the same as Column H of Table III:

$$S = -9.35\text{E-}4 \text{ NO2MAXL} \\ (2.12\text{E-}4) + 1.76\text{E-}4 \text{ NO2MAXH} + \text{other terms} \\ (0.81\text{E-}4)$$

Table VII. Comparison of Poisson and OLS models predicting illness duration.

	OLS		Poisson		$\frac{\partial S}{\partial x}$
	Coefficient	Std. error	Coefficient	Std. error	
Intercept	0.352	0.079 <sup>b</sup>	-1.62	0.361 <sup>b</sup>	
NO2MAXL	-0.00249	0.00056 <sup>b</sup>	-0.0083	0.0023 <sup>b</sup>	-0.00173 <sup>b</sup>
NO2MAXH	0.00043	0.000186 <sup>b</sup>	0.00195	0.00084 <sup>a</sup>	0.00041 <sup>a</sup>
PAR90P	-0.0047	0.00025	-0.00101	0.00120	-0.0021
SUL90P	-0.0026	0.0033	-0.0120	0.016	-0.0025
AGE	-0.0174	0.0023 <sup>b</sup>	-0.078	0.0102 <sup>b</sup>	-0.0162 <sup>b</sup>
CROWD	0.0089	0.0193	0.075	0.092	0.0156
EPIDEM	0.216	0.028 <sup>b</sup>	0.768	0.117 <sup>b</sup>	0.160 <sup>b</sup>
GAS	-0.032	0.031	-0.155	0.158	-0.030
RAIN	-0.0044	0.0042	0.0022	0.0195	0.00046
TEMP	0.0030	0.0011 <sup>b</sup>	0.0152	0.0052 <sup>b</sup>	0.0032 <sup>b</sup>
RACE1W	0.119	0.024 <sup>b</sup>	0.688	0.148 <sup>b</sup>	0.114 <sup>b</sup>
CHRON	0.091	0.016 <sup>b</sup>	0.399	0.069 <sup>b</sup>	0.093 <sup>b</sup>
CHESTINF	0.178	0.028 <sup>b</sup>	0.571	0.097 <sup>b</sup>	0.155 <sup>b</sup>

<sup>a</sup> Significant at the 5% level.<sup>b</sup> Significant at the 1% level.

with  $n = 14907$  and  $F = 25.1$  for the equation. This result indicated that the problem of autocorrelation could be ignored.

Contagion presented a problem that we were not able to resolve fully, due to a lack of complete information on all the physical contacts among the various members of the sample. However, we were able to examine contagion in the home, one of the most likely places where diseases may be spread.

If contagion in the home is present, the estimated effect on incidence and duration of variables common to members of a family, such as their exposure to air pollutants, will exceed the true effect. To test for this possibility we compared regression results from the full sample to the results from a subset consisting of one child chosen randomly from each family represented in the sample (Table VI). Although the standard errors on the former are a bit larger, (which is what one would expect from the reduction in sample size), the coefficients are quite similar. Thus, the results are probably not much affected by spread of disease in the home.

#### Limited Dependent Variables

In this section we examine whether the results depend on our use of OLS rather than techniques more suited to limited dependent variables. Specifically, we tested the linear probability model against a logit model for predicting illness incidence, using the "C" test described by Davidson and MacKinnon.<sup>22</sup> This test showed the logit model to be superior in the following sense: When the null hypothesis  $H_0$  is the

OLS model and the logit model is  $H_1$ .  $H_0$  is rejected; however, when the roles are reversed and  $H_0$  is the logit model,  $H_0$  cannot be rejected.

For illness duration a similar comparison was made between OLS and Poisson regression. Again, the OLS model was found to be inferior. Nonetheless, the coefficients on the independent variables estimated using OLS were very similar to the corresponding coefficients for the logit and Poisson models. These coefficients are compared in Tables VI and VII. To facilitate comparison, the rightmost column of each table is the derivative of the dependent variable of the Poisson or logit function, evaluated at the mean of the dependent variable. (For discrete independent variables the entry is the average change in probability of illness, estimated by the weighted sum of the change in probability when the variable is added at the mean and when it is taken away.) Even though OLS appeared slightly inferior to logit and Poisson regression in predicting illness incidence and duration, the qualitative results were hardly affected.

### Conclusions

A CHES data base from Chattanooga, Tennessee was thoroughly scrutinized and found to be of high enough quality to warrant epidemiological analysis. Using this data base, the relationship between  $\text{NO}_2$  ambient pollution levels and acute respiratory disease in children was examined. Although a statistically significant relationship was found, it was not monotonic. Indeed, over the range of pollution values experienced, more illness is associated with low pollution values than with high ones. A U-shaped relationship between illness and  $\text{NO}_2$  concentrations was found in several subpopulations in addition to the entire data set, although for some subpopulations no relationship was found. As far as we know, there is no clinical explanation for this result. In contrast, higher ambient sulfate levels were found to have a positive effect on acute respiratory disease incidence in children over the entire period and for different subsamples, although this effect was not significant for either season analyzed separately.

The strange relationship between  $\text{NO}_2$  concentrations and ARD in children could be attributable to three problems inherent in any epidemiological study. First, the relationship could be entirely fortuitous, although the odds against this for our study are long. Second, both illness and  $\text{NO}_2$  could be related to some unobserved variable. However, such a variable must have strange properties, because for certain well-defined subsets, its relationship to either illness or  $\text{NO}_2$  changes substantially. Finally, the data could still contain biases that create the observed effects.

In short, there is reason to be skeptical of a U-shaped dose-response function relating ambient  $\text{NO}_2$  levels and acute respiratory disease. Nonetheless, we suggest that non-monotonic dose-response functions be explicitly considered in future epidemiological or clinical research on the health effects of  $\text{NO}_2$  and perhaps other pollutants as well.

### Acknowledgments

This research was supported by the U.S. Environmental Protection Agency. We would like to thank David McLamb, Thomas Lareau, George Provenzano, and William Nelson of EPA, William J. Vaughn of the Inter-American Development Bank, and Clifford S. Russell of Resources For The Future for their encouragement and helpful comments. Victor Hasselblad of EPA deserves our special thanks for his assistance in data development. We also would like to thank our research assistant, Ruth Kazan. The usual disclaimer applies.

### References

1. M. D. Keller, R. R. Lanese, R. I. Mitchell, R. W. Cote. "Respiratory illnesses in households using gas and electricity for cooking." *Environ. Res.* 19: 495 (1979).
2. G. A. Lutz, R. I. Mitchell, R. W. Cote, M. D. Keller. "Respiratory Disease Symptom Study," prepared for American Gas Association by Battelle Columbus Laboratories, 1977.
3. R. J. W. Melia, C. du V. Florey, D. S. Altman, A. V. Swan. "Association between gas cooking and respiratory disease in children." *Br. Med. J.* 2: 149 (1977).
4. R. J. W. Melia, C. du V. Florey, S. Chinn. "The relation between respiratory illness in primary school children and the use of gas for cooking: (a) Results from a national survey, (b)  $\text{NO}_2$  respiratory illness, and lung infection (c) factors affecting  $\text{NO}_2$  levels in the home." *Int. J. Epidemiol.* 8: 347 (1979).
5. R. J. W. Melia, C. du V. Florey, R. W. Morris, B. D. Goldstein, D. Clark, H. H. John. "Childhood respiratory illness and the home environment I. Relations between nitrogen dioxide, temperature, and relative humidity." *Int. J. of Epidemiol.* 11: 155 (1982).
6. F. E. Speizer, B. Ferris, Y. M. M. Bishop, J. Spengler. "Respiratory disease rates and pulmonary function in children associated with  $\text{NO}_2$  exposure." *Am. Rev. Respir. Disease* 121: 3 (1980).
7. J. H. Ware, D. W. Dockery, A. Spiro, F. E. Speizer, B. G. Ferris. "Passive smoking, gas cooking, and respiratory health of children living in six cities." *Am. Rev. Respir. Disease* 129: 366 (1984).
8. J. Kagawa, T. Tayama. "Photochemical air pollution: its effects on respiratory function in elementary school children." *Arch. Environ. Health* 30: 117 (1975).
9. J. H. Stebbings, C. G. Hayes. "Panel studies of acute health effects of air pollution." *Environ. Res.* 11: 89 (1976).
10. W. S. Linn, J. D. Hackney, E. E. Pedersen, P. Breisacher, J. V. Patterson, C. A. Mulry, J. F. Loye. "Respiratory function and symptoms in urban office workers in relation to oxidant air pollution exposure." *Am. Rev. Respir. Disease* 114: 477 (1976).
11. C. A. Cohen, A. R. Hudson, S. L. Clausen, J. H. Knelson. "Respiratory symptoms, spirometry and oxidant air pollution in non-smoking adults." *Am. Rev. Respir. Disease* 105: 251 (1972).
12. C. M. Shy, G. J. Love. "Recent evidence on the human health effects of nitrogen dioxide." *Proceedings of the Symposium on Nitrogen Oxides*, American Chemical Society, Honolulu, Hawaii, 1979.
13. "Community Health and Environmental Surveillance System (CHES): An Investigative Report." U.S. Congress, House Committee on Science and Technology, 94th Cong., 2 Sess., 1976.
14. "Comments on Proposed EPA Nitrogen Oxides Ambient Air Quality Criteria." Roth Associates, Inc., for Utility Air Regulatory Group (UARG), Bethesda, Md., 1979.
15. A. J. Krupnick, C. W. Harrington. "Assessment of the Chattanooga Acute Respiratory Disease Survey: Phase I Report and Addendum." U.S. EPA, Office of Air Quality Planning and Standards, 1983.
16. L. J. Querec. "Comparability of Reporting Between the Birth Certificate and the National Utility Survey," in *Data Evaluation and Methods Research*, Series 3, no. 83; Public Health Service, DHEW Publication No. (PHS) 80-11357, 1980.
17. H. B. Wells, et al. "Completeness and Quality Response in the North Carolina Marriage Follow Back Survey," in *Data Evaluation and Methods Research*, Series 2, no. 56; Public Health Service, DHEW, 1973.
18. D. A. Belisle, E. Kuh, R. E. Welch. *Regression Diagnostics: Identifying Influential Data and Sources of Collinearity*, John Wiley & Sons, New York, 1980.
19. M. A. H. Russell, M. D. Lebowitz. "Environmental tobacco smoke. 4.2. Effects on health." *Eur. J. Respir. Diseases* 65: 140 (1984).
20. G. S. Maddala. *Limited Dependent and Qualitative Variables in Econometrics*, Cambridge University Press, Cambridge, MA, 1983.
21. T. Sawa. "Information criteria for discriminating among alternative regression models." *Econometrica* 46: 1273 (1978).
22. R. Davidson, J. G. MacKinnon. "Several tests for model specifications in the presence of alternative hypotheses." *Econometrica* 49: 781 (1982).
23. J. Kmenta. *Elements of Econometrics*, MacMillan, New York, 1971.

The authors are with Resources For The Future, 1616 P Street, N.W., Washington, DC 20036. This technical paper was submitted for peer review March 20, 1985; the revised manuscript was received July 16, 1985.

2023379718

**2023379719**

Watkins, C.J., Sittampalam, Y., Morrell, D.C., Leeder, S.R., Tritton, E. "Patterns of respiratory illness in the first year of life" British Medical Journal 293:794-796, 1986.

ABSTRACT: This paper describes a study of respiratory illness during the first year of life in a cohort of infants who were born between 1975 and 1978 to mothers who were registered with two inner London group general practices. The types of respiratory illness and their relation to the season of the year and season of birth of the child are examined. The relations among the frequency and type of respiratory illness and several social and family factors that have previously been shown to be associated with high levels of respiratory morbidity are also described.

2023379720



Details of self help groups are included in the newsletter. Usually between four and six groups function in the practice at one time. These have included relaxation, yoga for men, first time mothers, parents of teenagers, and groups for those who wish to lose weight or give up smoking. The newsletter also contains items of health information—for instance, on hypochloritis, flu jabs, taking your temperature, food labelling, and immunisations for holidays. Other items have included news of local changes, book reviews, articles on the history of the practice, details of fundraising events held by the Practice Participation Association, and local issues related to health.

The newsletter covers four sides of A4 paper. A typical front page is shown in the figure.

#### How is the newsletter distributed?

During 1982 the practice register was arranged geographically by volunteers to create a street index. It is thus possible to identify patients who live in a household, and labels are printed with the names of individual patients, one label per household. The task of reorganising the practice register of 11 500 patients geographically would probably occupy a full time person for about three weeks.

Two voluntary managers organise the distribution of newsletters to individual households. One hundred and twenty volunteers have been recruited by advertisements in the newsletter and in the surgery. Most deliver 50 to 100 newsletters in a geographically limited area, usually near their homes. To meet the requirements of the local medical community that the newsletter should not be construed as advertising for the practice, each newsletter is folded in three, leaving the outside largely blank, and sealed with an address label.

The cost of producing each edition of the newsletter is approximately £150. This is met by the association, which has a successful fundraising group. The cost is low only because of the enormous amount of voluntary help offered by members of the practice. The self adhesive address labels cost £45 to produce for each edition, and

this is met by the practice—the only cost to the doctors of the newsletter.

#### What does the newsletter achieve?

To assess what impact the newsletter has on members of the practice, a survey was carried out of patients' views of the newsletter. 178 patients who attended one of the surgeries and 42 patients who attended an open meeting of the association completed a questionnaire. Of these patients, 78% had heard of *Bringing Well*, most of whom knew that it was the newsletter of the practice association; 63% had read the last issue, though only 42% could remember a specific item in the last issue. Few patients made negative comments about the newsletter in the questionnaire, and no one has ever asked to be excluded from the delivery list.

There have been few spontaneous contributions from patients, but many people tell the deliverers that they welcome the newsletter, and several new patients have said how impressed they were by the evidence of community feeling in the practice. Delivering the newsletter is a simple task, and many people seem to enjoy having the opportunity to give something back to the practice in this way. Several have become group leaders or fundraisers, and the newsletter clearly performs an important nurturing role for the Practice Participation Association.

#### Conclusions

The practice newsletter has been produced regularly for three years with voluntary help, and thus the cost can be supported by the Practice Participation Association. Delivering it to households provides an unusual way of informing all members of the practice of the association's activities. It is hoped that the newsletter helps to promote a feeling among patients that they belong to a practice "community."

(Accepted 16 July 1986)

## Practice Research

### Patterns of respiratory illness in the first year of life

C J WATKINS, Y SITTAMPALAM, D C MORRELL, S R LEEDER, E TRUTTON

#### Abstract

This paper describes a study of respiratory illness during the first year of life in a cohort of infants who were born between 1975 and 1978 to mothers who were registered with two inner London group general practices. The types of respiratory illness and their relation to the season of the year and season of birth of the child are examined. The relations among the frequency and type of

respiratory illness and several social and family factors that have previously been shown to be associated with high levels of respiratory morbidity are also described.

#### Introduction

An association between various personal and family factors and an increased respiratory morbidity in children has been identified.<sup>1-3</sup> These community surveys have relied on the mothers' responses to questionnaires at interview about their infants' health to estimate the occurrence of respiratory illness. Such estimates have disagreed substantially with estimates derived from direct studies of respiratory illness in patients who have presented to attending general practitioners.<sup>4,5</sup>

Most serious respiratory illness in infancy is managed by general practitioners. Apart from the need for accurate diagnosis and effective treatment for the acute illness, the problem for the attending general practitioner is to identify and treat appropriately

Department of General Practice, United Medical and Dental Schools of Guy's and St Thomas's Hospitals, 11 Kruppington Road, London SE11 8SP  
C J WATKINS, MD, MRCP, senior lecturer in general practice  
Y SITTAMPALAM, MRCP, lecturer in medical statistics  
D C MORRELL, DM, MRCP, professor of general practice  
S R LEEDER, MD, MRCP, professor of community medicine, University of Sydney, Australia  
E TRUTTON, BM, BSC, research assistant

Correspondence to: Dr Watkins.

any respiratory illnesses that are likely to predispose to poor respiratory health in the future. Defining such illness is necessary before trials of alternative methods of treatment that are designed to improve prognosis can be carried out.

This paper describes the pattern of respiratory illness in children who presented to general practitioners during the first year of life and relates these to several family and social variables that have been found to be important determinants of respiratory health in children. A second paper relates measures of ventilatory capacity at the age of 5 to respiratory illnesses in the first year of life.<sup>2</sup>

## Methods

The study was done in two National Health Service groups practices situated in the same London borough of Lambeth. All children who were born to mothers who were registered with these practices between 1 June 1973 and 31 May 1978 were eligible for inclusion. To compare the socioeconomic characteristics of those who left the study practices during the first year of life with those who remained, all children who were enrolled were classified into social groups using a classification of residential neighbourhoods (ACORN) (CACE Market Analysis Division, London WC1V 6DR). This is a social classification based on the characteristics of areas of residence and requires only the identification of the individual's postcode to allocate the individual to a social group.

Throughout the first year of each child's life consultations with the general practitioner were recorded on special structured medical records. All consultations for respiratory illness the general practitioners recorded detailed clinical information on the present symptoms and physical signs. They distinguished five consultation types subsequent consultations in each episode of illness and were thus able to describe discrete episodes of respiratory illness. The records were checked for completeness by a research assistant after each consultation. At the child's first birthday a questionnaire was administered to the mother by a trained interviewer. This recorded the child's health during the first year of life, the health of the mother and father, and other social variables that were thought to have an important influence on the frequency of respiratory illness. The data were analysed using the regression techniques of the statistical package GLIM.<sup>3</sup> These techniques enable the effects of several factors to be examined simultaneously.

**Definition of respiratory illness.** Diagnostic labelling of respiratory illness is notoriously unsatisfactory.<sup>4-6</sup> This was confirmed in this study by postal standardized notes to the doctors, who differed widely in their diagnostic responses. The doctors, however, reliably identified five consultation types in episodes of illness and were consistent in whether they recorded the presence or absence of abnormal breath sounds or subnormalities of the chest. From these records upper and lower respiratory illness was defined as follows: (1) an episode of "upper" respiratory illness, so recording of abnormal lung sounds made at any consultation, or (2) an episode of "lower" respiratory illness, one or more consultations at which abnormal lung sounds were recorded.

## Results

Altogether, 54 infants were enrolled into the study. During the first year of the study, 132 (24%), moved away from the study practices. There was no significant difference between those who were lost to the study and those who remained with respect to sex and socioeconomic characteristics of areas of residence identified by the ACORN classification (see Methods). One infant died of a congenital at the age of three months. Of the children for whom there were complete consultation data, 404 (74%) of the mothers were interviewed at their child's first birthday.

Table 1 shows the frequency of consultations for episodes of respiratory illness. Only three children in the cohort were admitted to hospital with respiratory illness. Children with episodes of both upper and lower respiratory illness presented more frequently to surgery and earlier than to the summer months. Children with episodes of lower respiratory illness presented frequently during December, January, and February, with a peak in February in 1974, 1977, and 1978 and in March 1979.

Figure 1 shows the number of episodes of upper respiratory illness per 100 children over the four years of the study. For children born in the spring, summer, and autumn the incidence of upper respiratory illness peaked in the first winter after birth. Children who were born in winter appeared not to experience such upper respiratory illness in their first winter but showed a peak in the subsequent winter comparable to that for children who were born in other seasons of the year. Figure 2 shows the pattern of lower respiratory illness according to the season of the year in which the child was born. Again a winter peak occurred in lower respiratory illness for those children who were born in the spring, summer, and autumn. Children who

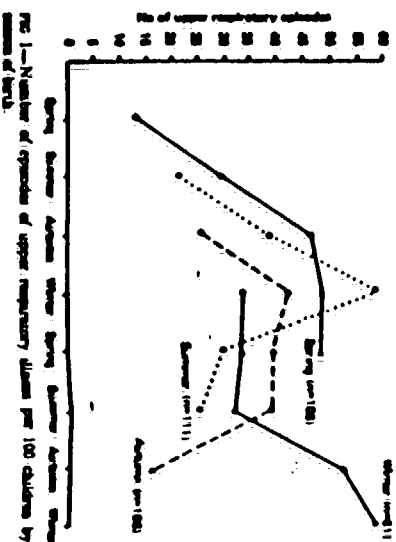


FIG. 1—Number of episodes of upper respiratory illness per 100 children by season of birth.

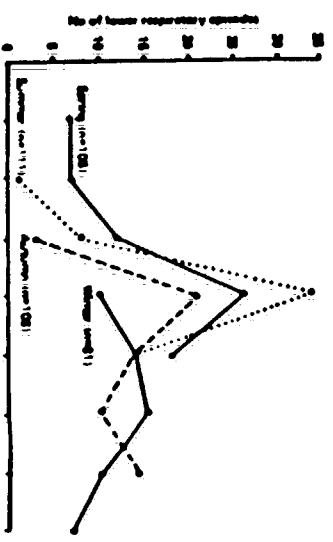


FIG. 2—Number of episodes of lower respiratory illness per 100 children by season of birth.

were born in the winter months had no peak incidence of lower respiratory illness in either their first or their second winter.

**Relation of upper and lower respiratory illness to episodes of non-respiratory illness.** There was no relation between the frequency of consultations for non-respiratory illness and the frequency of consultations for respiratory illness. High consulting rates for upper respiratory illness were not related to consultations for lower respiratory illness. This suggests that those children with high consultation rates for respiratory illness were not in high levels of medical care but that they experienced a much higher incidence of these illnesses.

## Relation of consultations for respiratory illness to social and family factors

Information was collected about several social and family variables that were found in previous studies to be associated with an increased frequency of lower respiratory illness (table II). The attack rate of respiratory illness was evenly divided between the sexes. For children of parents who were in manual occupations there was an attack rate of 37.5/100 for those whose parents worked in non-manual occupations. Lower respiratory illness was also reported more frequently in children who shared a room with an adult. Other factors associated with an increased frequency of consultations for lower respiratory illness included parental smoking, a probiotic drink in older parents' gas cooking in the home, sharing a room with another child, and parental symptoms of asthma. None of these was significant. In addition, no difference was found in this study for infants who were breast fed in terms of protection against lower respiratory illness.

To test the independence of effects of these social and family factors on frequency of lower respiratory illness in the first year of life, a multiple regression analysis was done using the factors listed in table II. The parents' occupation remained an important factor even when taking into account sharing a room with an adult and parental smoking. Attack rates of lower respiratory illness in children of parents in manual employment were estimated to be, from this model, 37.5/100 children; 5% confidence limits

immediately after birth. By the time they are exposed in the second round their defence mechanisms have matured sufficiently to

immediately after birth. By the time they are exposed in the second trimester, their defence mechanisms have matured sufficiently to protect them from infection. The role of immunity can be clarified only when simple methods of identifying viruses and of measuring the immune status of children become available for use in general practice. Studies carried out in hospital are unlikely to be helpful—only three of the 404 children in our study were admitted to hospital.

In this study the role of family health and social variables is not as clear cut as that reported by *Leander et al.*. The finding that the social class difference in frequency of consultation for respiratory illnesses, with high socioeconomic rates for those who fathers went to manual occupations. This is not explained by the fa-

[illegible]

cannot be explained by the many social and family variables examined in this study such as overworking, smoking habits

We thank the persons and the directors of the Lancaster Road Group Practice and the London Road Group Practice for providing the data for this study. Miss Mary Egan, Mr George Lewthal, and Mr Clive Murray for their help in data collection and analysis. Professor W. G. Holland, Professor Horne, Dr M. Pollock, and Mr D. Shabrook for their expert guidance on the design of the study, members of the department of occupational medicine (their comments on earlier drafts of this paper), and Mr Carmel Stephenson for patiently typing many drafts of this paper. The study was supported in part with a grant from the Department of Health and Social Security.

1000

2. Kasperk, G. S. (1984) *Journal of Paediatrics and Paediatric Surgery*, 19, 217.
3. Kasperk, G. S. (1985) *Journal of Paediatrics and Paediatric Surgery*, 20, 217.
4. Minkoff, H., Nishi, T., Bennett, A., Elliott, A. Factors affecting the rate of uterine regression after cesarean section. *Obstetrics and Gynecology*, 66, 254.
5. Coder, H.T., Raut, D.D. Uterine and breast organs of adolescent females in England and Wales. *British Medical Journal*, 191, 279.
6. Coder, H.T., Montgomery, D. The size of the uterine organ in a series of English schoolgirls. *British Medical Journal*, 191, 280.
7. Lander, S.E., Cornhill, D.L., Long, L.J., Melnick, J.L., Corder, H.T. Studies of uterine growth in adolescent females. *Journal of Paediatrics and Paediatric Surgery*, 1974, 19, 15.
8. Lander, S.E., Cornhill, D.L., Long, L.J., Melnick, J.L., Corder, H.T. Studies of uterine growth in adolescent females. *Journal of Paediatrics and Paediatric Surgery*, 1975, 20, 15.
9. Lander, S.E., Cornhill, D.L., Long, L.J., Melnick, J.L., Corder, H.T. Studies of uterine growth in adolescent females. *Journal of Paediatrics and Paediatric Surgery*, 1976, 21, 15.

10. Kervel JPC, de Lange AG. Missing information: respiratory distress and lung function in children. *Respiratory distress in children*, pp 44-67. Dordrecht, 1987: 11-16.
11. de Waard JC, van der Wal AC, de Waard JC. The respiratory distress syndrome in newborn infants. *Arch Dis Child* 1978; 53: 11-14.
12. de Waard JC, Linder SL, Gerkink BT. The respiratory distress syndrome and severe asphyxia in the first year of life. *J Paediatr Child Health* 1979; 15: 5.
13. Frenkel H, Wiedemann J. Clinical picture of neonatal respiratory distress and asphyxia in the first year of life. *Arch Dis Child* 1979; 54: 12-19.
14. de Waard JC, Borens P, Linder SL, van der Wal AC, Gerkink BT, Wiersma G. Clinical picture and natural course of neonatal respiratory distress in very premature. *J Pediatr* 1982; 101: 614-19.
15. Kervel JPC. The prevention and control of asphyxia in very premature. *J Pediatr* 1982; 101: 620-5.
16. de Waard JC, van der Wal AC, van der Wal AC. Outcome of respiratory distress occurring in the first year of life. *Arch Dis Child* 1981; 56: 67-71.
17. Madsen HA, Wiedemann JR, Linder SL. Controlled trial of surfactant. *Journal of the American Academy of Pediatrics* 1979; 64: 794-7.
18. Pappas F. Lung disease. London: Butterworth, 1979.

(Accepted 25 June 1981)

## References

1. Wadkin JM. Secondary problems and their consequences from a respiratory disease. *Respiratory Diseases: A Synopsis of Classification, 1984*. New York: McGraw-Hill, 1984: 103-11.
2. Lane JT, Karamanou J, Matarazzo AJ. Patterns of respiratory illness in England: socioeconomic, demographic and environmental influences. *Int J Epidemiol* 1987; 16: 211-17.
3. Mulcahy DM, Mulcahy T, Bennett AJ, Elliott A. Factors affecting the onset of chronic respiratory disease. *Br Med J* 1989a; 39: 954.
4. Coker JE, Mulcahy DM. Ulcers and other signs of endothelial dysfunction in cigarette smokers. *Br Med J* 1989b; 399: 1165.
5. Coker JE. Respiratory disease in smokers. *Br Med Bull* 1991; 37: 9.
6. Bland JM, Mulcahy DM. The relationship of respiratory symptoms to a history of lung disease. *Br Med J* 1991; 303: 1105-8.
7. Lander EH, Curbishell BT, Long GL, Mulcahy DM, Curbishell BT. Lung biopsy in cigarette smokers: evidence for the presence of the Alveolar septal interstitial pneumonia. *Am Rev Respir Dis* 1991; 143: 1315-21.
8. Wain JN, Perry CMV, Abbing DG, Long AV. Alveolar septal interstitial pneumonia: a syndrome. *Br Med J* 1977; 334: 101-15.
9. Kuperoff MD, Long AV. Histologic evidence: respiratory disease and lung function in patients with a South West Coast syndrome of Pneumonia and Small Airways Disease. *Am Rev Respir Dis* 1980; 121: 113-4.
10. Wadkin JM, Lander EH, Curbishell BT. The relationship between lung and heart disease in cigarette smokers. *Am Rev Respir Dis* 1981; 123: 1185-7.
11. Titterton JE, Wadkin JM. Coughing in healthy cigarette smokers and cigarette smokers with respiratory disease in the lung (in press).
12. Wadkin JM, Wadkin JM. Coughing in healthy cigarette smokers and cigarette smokers with respiratory disease and interstitial disease in the lung (in press).
13. Wadkin JM, Curbishell BT, Lander EH, Mulcahy DM, Curbishell BT. Lung biopsy in cigarette smokers: evidence for the presence of the Alveolar septal interstitial pneumonia. *Am Rev Respir Dis* 1991; 143: 1315-21.
14. Wadkin JM, Curbishell BT, Lander EH, Mulcahy DM. Outcome of respiratory disease occurring in the lung (in press).
15. Mulcahy DM, Wadkin JM, Curbishell BT. The relationship between lung and heart disease in cigarette smokers. *Am Rev Respir Dis* 1981; 123: 1185-7.
16. Ferguson P. Lung cancer. In: *Blackwell, London Textbook*, 1999.

2023379724

Kerigan, A.T., Goldsmith, C.H., Pengelly, L.D. "A Three-Year Cohort Study of the Role of Environmental Factors in the Respiratory Health of Children in Hamilton, Ontario" American Review of Respiratory Disease 133: 987-993, 1986.

SUMMARY: The relative importance of the effect of outdoor environmental factors (suspended particulates, sulphur dioxide) and indoor environmental factors (parental smoking, gas cooking) on the respiratory health of children is still unclear. To answer these questions, a 3-yr cohort analytic study has been conducted in Hamilton, Ontario between 1978 and 1981. The prevalence of respiratory symptoms and indoor environmental factors was determined by an interviewer-administered questionnaire. Pulmonary function measures included both the forced expiratory maneuver and the single- and multiple-breath nitrogen washouts. Outdoor air quality was measured by a comprehensive network of suspended particulate and sulphur dioxide monitors. There were 3,345 children 7 to 10 yr of age studied in the first year; a response rate of 95.4%, 3,727 in the second year, and 3,168 in the third year; 75.6% of the initial cohort were studied in both Year 2 and Year 3. Comprehensive quality control in the study included measurement of the repeatability of both the questionnaire and pulmonary function data. Repeatability was acceptable except for variables derived from the single-breath nitrogen washout (correlation between initial and repeat closing volume vital capacity was 0.14). Cigarette smoking in Year 3 was reported in 4.8% of the children. The distribution of other covariables was not uniform, and the prevalence of parental smoking and gas cooking was greatest in the industrial area with the highest particulate pollution. Future analysis of these data will require the effect of these covariables to be distinguished from that caused by outdoor air pollution.

2023379725

# A Three-Year Cohort Study of the Role of Environmental Factors in the Respiratory Health of Children in Hamilton, Ontario

## Epidemiologic Survey Design, Methods, and Description of Cohort<sup>1-3</sup>

ANTHONY T. KERIGAN, CHARLES H. GOLDSMITH, and L. DAVID PENGELLY

### Introduction

The study of environmental factors responsible for respiratory disease in children is important for 2 reasons: (1) the absence of confounding factors, such as personal smoking and occupation, makes the interpretation of any observed association between air quality and respiratory disease more credible; and (2) the growing realization that respiratory illness during childhood may predispose to the development of respiratory morbidity and early mortality from respiratory illness during adult life (1, 2).

This particular usefulness of children has become more important as air quality has improved during the last decade (1970-1979) and levels become closer to the Ontario guidelines. For total suspended particulates (TSP), the Ontario objective (annual geometric mean) is 60  $\mu\text{g}/\text{m}^3$ . In 1978, the annual TSP in Hamilton was 77  $\mu\text{g}/\text{m}^3$ . For sulphur dioxide, the objective is 0.02 ppm annual average and the measured level was 0.016 ppm (3).

Studies in several countries from 1967 to 1978 have identified a number of environmental factors that might lead to respiratory disease in children. The initial study of the effect of the particulate/sulphur dioxide ( $\text{SO}_2$ ) complex was conducted by Lunn and coworkers (4) and showed increased prevalence of respiratory symptoms and reduced pulmonary function in areas of poor air quality. Improvement in air quality led to a reduction in these adverse health effects (5). Follow-up studies in several towns in the United Kingdom by Melia and colleagues (6) showed that adverse health effects were now extremely difficult to find with the further improvement in air quality. These studies, however, did not consider the possible role of parental smoking.

As outdoor air quality improved, at-

**SUMMARY** The relative importance of the effect of outdoor environmental factors (suspended particulates, sulphur dioxide) and indoor environmental factors (parental smoking, gas cooking), on the respiratory health of children is still unclear. To answer these questions, a 3-yr cohort analytic study has been conducted in Hamilton, Ontario between 1978 and 1981. The prevalence of respiratory symptoms and indoor environmental factors was determined by an interviewer-administered questionnaire. Pulmonary function measures included both the forced expiratory maneuver and the single- and multiple-breath nitrogen washouts. Outdoor air quality was measured by a comprehensive network of suspended particulate and sulphur dioxide monitors. There were 3,945 children 7 to 10 yr of age studied in the first year, a response rate of 95.4%, 3,727 in the second year, and 3,168 in the third year; 75.8% of the initial cohort were studied in both Year 2 and Year 3. Comprehensive quality control in the study included measurement of the repeatability of both the questionnaire and pulmonary function data. Repeatability was acceptable except for variables derived from the single-breath nitrogen washout (correlation between initial and repeat closing volume vital capacity was 0.14). Cigarette smoking in Year 3 was reported in 4.8% of the children. The distribution of other covariables was not uniform, and the prevalence of parental smoking and gas cooking was greatest in the industrial area with the highest particulate pollution. Future analysis of these data will require the effect of these covariables to be distinguished from that caused by outdoor air pollution.

AM REV RESPIR DIS 1985; 133:987-993

tention changed to indoor air quality, particularly in relation to parental smoking and indoor sources of gaseous pollutants such as gas stoves. The health effects from parental smoking appear to be most marked in the first years of life (7), but studies of this effect on older children have not yielded consistent results, some showing increased prevalence of symptoms (8) but others showing no effect (9, 10). Colley and coworkers (11) suggested that the effect of parental smoking may be due predominantly to the increased prevalence of parental cough. An effect of parental smoking on children's pulmonary function has also been shown (12, 13). The influence of gas cooking was first suggested by Melia and coworkers (14), although the effect seemed to decrease as the children became older. In contrast, Keller and colleagues (15) were not able to find any effect of gas cooking on children's respiratory symptoms.

The uncertainty about the role of low levels of TSP and  $\text{SO}_2$ , and their importance in relation to domestic environmental factors, led us in 1978 to initiate a 3-

yr cohort study in Hamilton, Ontario that was designed to answer the following questions. (1) Is there an effect on children's respiratory health of suspended particulates and  $\text{SO}_2$  at the present levels? (2) What is the effect of the various factors in the domestic environment when considered in relation to outdoor air quality?

The main study was preceded by a pi-

(Received in original form January 14, 1985 and in revised form July 19, 1985)

<sup>1</sup> From the Departments of Medicine and Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario, Canada.

<sup>2</sup> Supported by National Research and Development Programme Project No. 6606-1752-53 from Health and Welfare, Canada, by Project No. 78-020-33 from the Ministry of Environment, Ontario, and by Public Health Grant No. CHS-R34 from the Ministry of Health, Ontario.

<sup>3</sup> Requests for reprints should be addressed to Dr. A. T. Kerigan, Urban Air Environment Group, McMaster University, Room 3E27, Health Sciences Centre, 1200 Main Street West, Hamilton, Ontario, L8N 3Z5, Canada.

2023379726

TABLE 1  
SUSPENDED PARTICULATE LEVELS BY AREA OF CITY  
(JANUARY THROUGH DECEMBER 1980)

	WU	EU	WL	EL	IC
Total suspended particulates, $\mu\text{g}/\text{m}^3$ <sup>a</sup>	44	43	61	58	90
TSP Load < 7.0 $\mu$ , %	70.3	66.8	67.9	71.1	62.1
Maximal daily average, $\mu\text{g}/\text{m}^3$ <sup>b</sup>	140	146	173	149	223
Monitoring sites, n	5	3	9	4	5

Definition of abbreviations: WU = west upper quadrant; EU = east upper quadrant; WL = west lower quadrant; EL = east lower quadrant; IC = industrial core.

<sup>a</sup> Average of annual geometric means of all sites in each area.

<sup>b</sup> Average of daily maxima of all sites in each area.

lot study (16) which demonstrated that within Hamilton, Ontario, there existed substantial gradients across the city for suspended particulates and  $\text{SO}_2$  that would enable us to study children with differing exposures in the same city. This offered major logistical advantages in a design similar to that of Lunn and co-workers (4). During the current study, these gradients for suspended particulates continued to be present. The levels in each area of the city during 1980 are shown in table 1 in terms both of the annual geometric mean and of the daily maximum. The table also shows the proportion of particulate load less than 7.0  $\mu$ . Despite the increasing level of particulates towards the industrial core, there is little change in the proportion of particulate matter less than 7.0  $\mu$ .

## Methods

### Design of Study

Hamilton, with a population of approximately 300,000, is a city situated at the western end of Lake Ontario. The dominant geographic feature is an escarpment of approximately 100 m high that runs from east to west, effectively dividing the city into a lower section and a mountain section. The city is industrial, with the heavy industrial core, located in the northeast section of the city, being the dominant producer of particulate and  $\text{SO}_2$  emissions, although there is a secondary  $\text{SO}_2$  area source in the commercial section located in the western part of the city. Prevailing winds are from the southwest.

Initial air quality monitoring during the pilot study had indicated the presence of substantial gradients for both particulates and  $\text{SO}_2$ , with the mountain section having lower levels than the lower section of the city. On this basis and on the knowledge of prevailing winds, we divided the city into 4 quadrants (figure 1) for the purpose of selection of the sample to be studied. The sampling frame was all public elementary schools within the city of Hamilton. Sample size considerations dictated that at least 800 children would be required within each quadrant. A difference of 5 to 7% in the mean of a particular pulmonary function variable was felt to be neces-

sary for biologic significance. One of the principal outcomes of interest was the measurement of air flow, especially at low lung volumes. Estimates of the mean and standard deviation of these variables were obtained from our pilot study (16) ( $\text{FEV}_{1.0}$ : mean, 1.79 L; SD, 0.36;  $\text{MEF}_{75}$ : mean, 1.09 L/s; SD, 0.44). The first criterion employed in sample size determination was that there should be only a 10% chance of missing a biologic difference (Beta error = 0.1). A second criterion was that a difference was considered to exist between the 2 samples if the appropriate statistical test showed that the observed difference had only a 5% chance of occurring in the absence of any real difference (Alpha error = 0.05). Within each of these quadrants, schools were randomly selected until at least 800 children from Grades 2, 3, and 4 during the initial school year had been included. The only children excluded were those older than 10 yr of age by the end of 1978. All children in the required grades from the final school selected in each quadrant were chosen. The children included in the first year of testing made up the initial cohort.

After more detailed air quality monitoring during the first year of the study, it was realized that the area of highest exposure (i.e., TSP annual geometric mean  $> 60 \mu\text{g}/\text{m}^3$ ) was underrepresented, despite the initial stratification by quadrants in the original design. For this reason, the 3 remaining schools in this area were added, with all children within the required age interval being included.

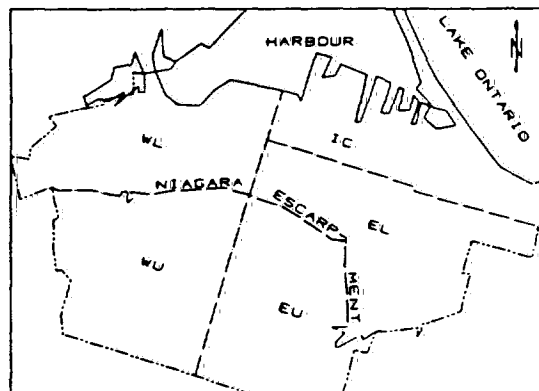
In addition, in the second year, all children

in this same age interval as the initial cohort who moved into a school of study were included in the study. During the third year, no new children were added.

The questionnaire used in the study was one that we had employed in the pilot study. It was developed from a questionnaire used in a similar study in the European Economic Community. The questionnaire covered several aspects of the child's respiratory history, family smoking and respiratory profile, certain aspects of the child's medical background, and information relating to the quality of the dwelling and socioeconomic circumstances of the family. There were differences between our questionnaire and that developed by the American Thoracic Society (17). In our questionnaire, a distinction was made between morning cough and cough during the day or night, the respondent being asked if the child usually coughed in the morning or during the day or night, respectively. Sputum production was not asked about. The question on wheezing inquired if the chest ever sounded wheezy or whistling. In addition, a question about asthmatic attacks in the previous 12 months was included. Two questions related to acute respiratory illness were included. The first asked about a period of cough and phlegm lasting for 3 wk or more and the second about any chest illness keeping the child home for a week or more. (A detailed questionnaire is available from the writers.) In Year 2, questions about early childhood illnesses were added that were derived from the questionnaire designed by the American Thoracic Society (17). Our questionnaire was administered in the home by a trained interviewer to the mother or female guardian, or in her absence, to the father or male guardian. The questionnaire was administered in each of the 3 yr of the study prior to the performance of pulmonary function testing.

Pulmonary function testing was performed at the child's school. Four types of pulmonary function tests were performed: forced expired maneuvers ( $\text{FEV}_{1.0}$ , FVC,  $\text{MEF}_{75}$ ,  $\text{MEF}_{50}$ , and MET), spirometry (a slow vital capacity (VC) following quiet breathing) (VC, ERV), single-breath nitrogen washout (CV/VC,  $\text{N}_2$  difference) and multiple-breath

Fig. 1. Outline map of Hamilton, Ontario, showing the 4 quadrants chosen in the original design, and the Industrial Core (IC) (WU = west upper; EU = east upper; WL = west lower; EL = east lower).



nitrogen washout (FRC). The additional use of the single-breath nitrogen washout was justified by the study of Becklake and coworkers (18), who showed an increase in closing volume in children exposed to a high particulate/SO<sub>2</sub> environment.

Air quality was measured by a comprehensive particulate and SO<sub>2</sub> network. There were 27 monitored sites for TSP using hi-vol samplers, with 9 additional hi-vol samplers with Andersen 4-stage cascade impactors for the measurement of mass median diameter. In addition, there were 16 sites for SO<sub>2</sub> monitored in groups of 8, using Beckman 906A monitors (Beckman Instruments, Fullerton, CA), for 6-wk periods in rotation. These sites were distributed throughout the city. Details of air quality monitoring will be contained in a subsequent report.

#### Protocol

In the questionnaire survey, interviewers were randomly assigned to eligible children at each school to be visited, thus ensuring that several interviewers would be assigned to each school. In addition, interviewers were rotated to schools in different parts of the city. The parents had been informed in advance by letter to expect a phone call from the interviewer. The letter also described the purpose of the study as being the investigation of the child's respiratory health. No mention was made of air pollution. Each interviewer telephoned the parent or guardian to arrange for an appointment for questionnaire administration. There was provision for 3 call-backs, if no contact was established initially, before no further attempt at interviewing was made. At the time of contact, the interviewer was able to screen out those children who were older than 10 yr of age in the first year of testing. If the parent consented to the interview, they were then visited by the interviewer. The percentage of those eligible, for whom an interview was not obtained, including those with whom no contact could be established, ranged from 4.6% in Year 1 to 3.3% in Year 3 (table 2). No further attempt was made to follow these. Interpreters were used as necessary, but were required for less than 1% of the parents. At the end of the interview, the pulmonary function test was explained to the parent or guardian, and written consent for the test was obtained at that time. The completed questionnaire was then returned for coding, keypunching, and data storage at the Computation Services Unit at the Health Sciences Centre, McMaster University.

Pulmonary function testing was performed, throughout the school year, within 4 wk of the completion of the interview. Two teams of pulmonary function technicians were assigned alternately to a school in the upper and in the lower part of the city. The testing routine was explained initially to all the students at an assembly and explained further to each child at the time of his or her testing. A questionnaire about smoking habits was also administered to the child at the time of testing in the third year of the study. Pulmo-

TABLE 2  
CONSENT AND TESTING RATE FOR SAMPLE

	Year 1	Year 2	Year 3
Eligible for interview	3,505	3,727	3,168
Interviews completed	3,345	3,588	3,065
Interview completion rate, %	95.4	96.3	96.7
Consents given for testing	3,329	3,573	3,055
Consent rate, %	95.0	95.9	96.4
Number tested	3,131	3,439	2,949
Testing completion rate, %	89.3	92.3	93.1

nary function testing was performed using the Hewlett-Packard 47804A Pulmonary Calculator System (Hewlett-Packard, Waltham, MA). In this system, flow is measured by a pneumotachygraph, and volume is computed internally by integration with time. Calibration of the 2 systems used was performed twice daily with a 2-L syringe. Correction for ambient temperature and pressure was performed internally by the computer system by entering the appropriate values. After measurement of height and weight, the child first performed a multiple-breath nitrogen washout. This was followed by at least 3 forced expired maneuvers. For acceptance, the 2 largest FVC values had to be within 5% of each other. All measurements were taken from the maneuver with the greatest sum of FVC and FEV<sub>1</sub>. Spirometry was then performed. If the VC obtained was less than the FVC by more than 10%, the spirometry was repeated until the estimate was within 10%. However, if the VC was greater than the FVC by more than 10%, then the forced expired maneuver was repeated until the FVC estimate was within 10% of VC. Finally, at least 2 single-breath nitrogen washouts were performed in which the expired nitrogen concentration was continuously plotted against VC. The method used was that of Mansell and associates (19), but without the additional dead space. For acceptance of the single-breath nitrogen washout test, the VC had to be within 10% of the largest previous VC from spirometry. If both single-breath maneuvers were acceptable, then the closing volume from the maneuver with the greater VC was taken for analysis. The presence of an upper or lower respiratory infection was noted by the technician at the time of the test. However, the test was always performed, the infection data to be used at the time of analysis to estimate the effect of the infection on pulmonary function. The testing followed the same sequence in Years 2 and 3, except that in Year 3, the single-breath nitrogen washout was omitted because of poor reproducibility (see Discussion). The child was not necessarily tested with the same system nor by the same technician, but comparison of results from the 2 teams was performed at regular intervals to identify any systematic differences.

All measurements of flow and of volume were computed internally, with output being recorded by an on-line printer. Closing volume, however, was computed by inspection

of the single-breath nitrogen washout curve, and was taken at that point of inflection of the nitrogen washout curve from a line drawn through phase 3 of the curve (19). These results were then returned for coding, keypunching, and data storage in a manner similar to the questionnaire data.

The quality control of the data gathered was performed in several ways. For both the questionnaire and the pulmonary function coding, a random 5% sample of the data was recoded by a second coder. The reliability of the questionnaire data was estimated by the random selection of 4 interviewers after each pair of schools was completed. For each interviewer, 2 interviews were randomly chosen, and within those interviews, 2 questions were randomly selected. The appropriate respondent was then phoned and the questions were asked again. Apart from estimating the reliability of the answers, this procedure also verified that the original interview had indeed taken place. Interinterviewer variation or bias was estimated by comparing the response rates to certain questions obtained by each interviewer. These data were then examined to see if any differences between interviewers might be greater than that caused by chance alone. When such a difference was found, interviewing technique was reviewed to ensure consistency of technique. In no case was it necessary to change any of the interviewing staff because of poor reliability.

The reliability of the pulmonary function testing was estimated by the retesting of 8 children in each school, 2 children randomly chosen from each age group. All data from pulmonary function testing were passed through a range checking program after data storage, the range being 4 standard deviations centered at the mean, these interval estimates of parameters being derived from the original pilot study. Finally, we were interested in determining any systematic differences between the 2 pulmonary function testing teams. The presence of any differences was estimated by parallel line regression analysis for 4 of the variables measured (FVC, ME<sub>F</sub>, MET, and CV/VC). This technique used regression analysis to fit a regression line separately to the data collected by each team; if the linear relationship was the appropriate model, then the hypothesis that the 2 lines were parallel was tested. If this hypothesis was not rejected, then the hypothesis that the intercepts were the same was tested. If the second hypothesis was

2023379728



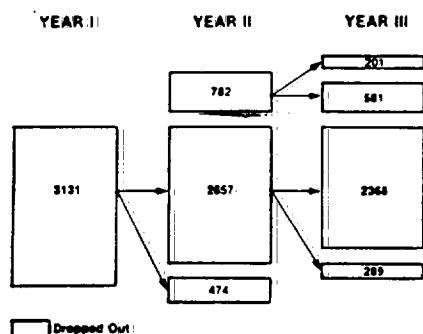


Fig. 2. Maintenance of cohort size, showing numbers lost by attrition and Industrial Core group added during Year 2.

not rejected then it was concluded that the regression lines for the 2 teams were coincident (20).

A final quality control measure was an examination of the proportion of missing values for each variable for each team, as an indicator of systematic differences between the 2 teams. The analysis and the results of these quality control measures will be described in detail in a separate report. However, the reliability of the questionnaire and pulmonary function data, and the success rates of pulmonary function testing, are described in this report.

Statistical analyses were performed by subprograms in the Statistical Package for the Social Sciences (21). The difference between sample means was tested for significance by subprogram *t* test for paired samples. Pearson's product-moment correlation coefficient, as a measure of association of 2 independent variables, was computed by subprogram scattergram. Hypothesis tests were all two-tailed.

## Results

### Characteristics of Cohort

The number who were eligible for testing in each year of the study is shown in table 2. To be eligible, the child could

not have attained his or her eleventh birthday before December 31, 1978. This table also shows the interview completion rate obtained in each year. The rate, which was above 95% for each year, is considered acceptable. In addition, the percentage giving consent for the pulmonary function testing was virtually identical to that giving consent for interview. There was, however, a degree of attrition after consent was given for pulmonary function testing, before the test was performed. The major reason for this was the child having moved from a testing school into a nontesting school during the time between consent and testing. This attrition was less in Years 2 and 3.

An important feature of the study was

the ability to follow the initial cohort into the second and third years of the study. The particular importance of this is the ability to measure changes in pulmonary function variables as the child grows. It is possible that the rate of change of a particular pulmonary function variable might be a more sensitive outcome measure than the use of a single point estimate. The number of children with pulmonary function testing in Year 1 who were tested in Years 2 and 3 (approximately 75% of the original cohort) is shown in figure 2. The figure also shows the number of children added in Year 2 and how many of these were followed into Year 3. The characteristics of the children at the time of pulmonary function

TABLE 3  
CHARACTERISTICS OF SAMPLE TESTED

	Year 1		Year 2		Year 3	
	(n)	(%)	(n)	(%)	(n)	(%)
Male	1,611	51.5	1,789	51.4	1,513	51.3
Female	1,520		1,670		1,436	
Caucasian	2,876	91.9	3,161	91.9	2,723	92.3
Non-Caucasian	255		278		226	
Total	3,131		3,439		2,949	

TABLE 4  
PREVALENCE OF DOMESTIC FACTORS BY AREA OF CITY: YEAR 2\*

	WU	EU	WL	EL	IC
Number	829	878	741	863	242
Mother smoke	37.3	42.5	42.2	48.2	60.1
Father smoke	38.3	43.4	43.3	50.2	61.3
Mother cough	15.7	15.0	17.8	17.5	28.5
Father cough	22.1	26.4	26.1	25.6	40.4
Gas cooking	8.3	8.3	29.7	15.6	43.4
Share room with 2 or more	2.3	3.6	7.3	7.0	8.8
Income less than \$10k/yr	15.8	11.3	20.7	15.6	25.9
Less than 2 yr at present address	22.4	19.0	28.2	25.6	34.4

For definition of abbreviations, see table 1.

\* Values are percentages. Data missing on 35 subjects.

TABLE 5  
PREVALENCE OF SMOKING\*

	Age (yr)						Total
	8	9	10	11	12	13	
Any history of smoking†							
Yes	0 (0)	57 (11.8)	175 (18.1)	250 (28.3)	188 (37.8)	37 (50.0)	707 (24.3)
No	3	425	791	634	310	37	2,200
Total	3	482	966	884	498	74	2,907
Smoking in last 4 wk‡							
Yes		2 (3.6)	28 (16.4)	41 (17.0)	56 (30.8)	12 (32.4)	139 (20.3)
No		53	143	200	126	25	547
Total		55	171	241	182	37	686

\* Values are frequency with percentages in parentheses.

† Missing observations, 158.

‡ Missing observations, 21.

TABLE 6  
REPEATABILITY OF RESPIRATORY SYMPTOM QUESTIONS

Question	Raw Agreement	Chance-Corrected Agreement (Kappa)
Cough in morning	0.92	0*
Cough during day or night	0.80	0*
Chest wheezy or whistling	0.80	0.53
Asthma in previous 12 months	0.96	0.76
Cold goes to chest usually	1.0	1.0
Cough and phlegm for 3 wk in previous 12 months	0.95	0*
Absence from school for 1 wk or more in previous 12 months	1.0	1.0

\* In each case, one marginal was zero, making Kappa an unreliable estimate of chance-corrected agreement.

testing in each of the 3 yr are shown in table 3. There is a slight excess of males over females in each year, and the predominant Caucasian ethnic characteristic of the sample is to be noted.

Previous studies have shown that certain factors other than outdoor air quality can be related to the incidence or prevalence of childhood respiratory disease (7, 10, 13). The distribution of these factors in each of the 4 original quadrants, and also in the additional group of schools in the industrial core that were added in Year 2, are shown in table 4. In this table, a smoker is one who smokes 1 or more cigarettes or cigars per day. The percentage with cough includes those with a positive answer to either of the questions: "Do you usually cough in the morning?" or "Do you usually cough during the day or night?" To simplify the presentation, only the results from Year 2 are shown. However, those from Years 1 and 3 are similar. The prevalence of these factors varied across the city and was highest in the industrial area, where the level of TSP was also the highest (table 1). A further, potentially confounding covariable was the prevalence of smoking by the children themselves. Because the age interval in the first year was between 7 and 10 yr of age, we did not expect to find many smokers. However, by the third year of the study, it might be expected that some of the older children would have commenced regular smoking. We therefore administered a smoking questionnaire to the children at the time of pulmonary function testing. The number of children in each age group who stated that they had smoked at least 1 cigarette in the last 4 wk is shown in table 5.

#### Quality Control

The repeatability of the respiratory symptom questions is shown in table 6, which

details the agreement statistics for each of these questions, both in terms of raw agreement and of chance-corrected agreement (Kappa). In certain cases, Kappa was an unreliable estimate of chance-corrected agreement, because one marginal of the  $2 \times 2$  table from which the Kappa was to be computed was zero. Kappa ranged from a substantial level of 0.56 to an excellent level of 1.0. The per-

centage of missing values by team for variables derived from the 4 pulmonary function maneuvers is shown in table 7. The values are shown for Year 1. The commonest reason for a pulmonary function value to be missing was that the child could not meet the required criteria for test acceptance. These results, therefore, give a comparison of ability of the 2 teams in obtaining successful tests for each test in each age group. The repeatabilities of the lung function measurements in Years 1 and 2 of the study are shown in tables 8 and 9. There were small but significant differences for several of the measurements (FVC,  $MEF_{50}$ ,  $MEF_{75}$ , MET, and VC) in Year 1 and to a larger extent in Year 2. The results for Year 3 are not displayed for sake of brevity, but they showed no significant differences. The product-moment correlation coefficients for certain of these variables are shown in table 10 for Year 1. These range from 0.97 for FVC to 0.14 for CV/VC. The reproducibility of these tests might have been affected by the presence of a respiratory infection during either the ini-

TABLE 7  
PERCENTAGE OF MISSING VALUES BY TEAM: YEAR 1

Variable	Team	Age (yr)						Total
		6	7	8	9	10	11	
FVC	A	0.0	1.0	0.4	2.1	0.3	2.6	1.0
	B	0.0	3.3	1.6	1.3	0.9	3.4	1.8
VC	A	33.3	12.5	5.1	7.5	1.0	0.0	6.4
	B	33.3	11.5	5.4	2.4	1.8	3.4	5.1
FRC	A	16.7	5.8	3.9	4.8	1.0	0.0	3.9
	B	16.7	10.4	5.0	1.5	1.3	3.4	4.4
CV	A	66.7	49.0	28.6	23.8	12.6	5.1	27.7
	B	33.3	37.4	24.2	14.3	9.0	20.7	21.2
$N_2$ difference	A	66.7	49.3	28.8	23.8	12.6	5.1	27.9
	B	33.3	38.5	24.2	14.0	9.0	20.7	21.3
Children tested, n	A	6	304	532	480	288	39	1,647
	B	6	270	501	456	223	29	1,485

Definition of abbreviations: CV = closing volume;  $N_2$  difference = increase in expired nitrogen concentration during phase III of single-breath nitrogen washout.

TABLE 8  
REPEATABILITY OF LUNG FUNCTION MEASUREMENTS: YEAR 1

Variable	n	Initial		Repeat		t Value	p Value (2-tailed)
		Mean	SD	Mean	SD		
FVC	216	2.04	0.41	2.07	0.41	-3.96	< 0.001
FEV <sub>1</sub>	216	1.67	0.31	1.68	0.31	1.33	0.190
$MEF_{50}$	215	2.33	0.62	2.14	0.59	3.57	< 0.001
$MEF_{75}$	211	0.99	0.38	0.94	0.32	3.45	0.001
MET	215	0.57	0.17	0.59	0.16	-3.13	0.002
VC	220	2.05	0.41	2.08	0.40	-3.30	0.001
FRC	210	1.19	0.31	1.19	0.29	0.13	0.895
CV/VC	166	0.134	0.09	0.12	0.078	1.42	0.158
$N_2$ diff	160	1.04	0.66	1.03	0.52	0.13	0.900

Definition of abbreviations: MET = midexpiratory time in seconds. For other definitions, see table 7.

TABLE 9  
REPEATABILITY OF LUNG FUNCTION MEASUREMENTS: YEAR 2

Variable	n	Initial		Repeat		t Value	p Value (2-tailed)
		Mean	SD	Mean	SD		
FVC	256	2.37	0.47	2.35	0.51	2.24	0.026
FEV <sub>1</sub>	256	1.91	0.36	1.88	0.39	2.66	0.008
MEF <sub>50</sub>	254	2.46	0.63	2.39	0.66	2.64	0.009
MEF <sub>75</sub>	254	1.05	0.34	1.03	0.35	1.49	0.138
MET	256	0.59	0.16	0.60	0.19	-1.79	0.75
VC	255	2.39	0.47	2.36	0.49	2.37	0.019
FRC	253	1.32	0.33	1.31	0.34	0.37	0.713
CVVC	226	0.12	0.08	0.12	0.09	-0.13	0.897
N <sub>2</sub> diff	226	0.88	0.50	0.85	0.44	1.35	0.178

For definition of abbreviations, see tables 7 and 8.

tial or the repeat test. The repeatabilities of the lung function measurements were therefore reanalyzed, omitting from the analysis any test during which the presence of an upper or lower respiratory infection had been recorded. The results from this analysis are shown in table 11. Comparison with table 9 does not indicate that the reproducibility of the test was improved by the exclusion of current respiratory infections. In addition, for no variable was the product-moment correlation coefficient changed by the exclusion of respiratory infections.

#### Discussion

This report outlines the background to the study that has been undertaken, the design of this study, and the methods that were used, and it describes the sample that was studied, both in terms of its characteristics and also in terms of important covariables. The design of the study was innovative in selecting schools within each of 4 quadrants of the city in expectation that these areas would show different levels of air quality. However, the area of the city with TSP levels greater than 60  $\mu\text{g}/\text{m}^3$  annual geometric mean was underrepresented when the air quality results from the first year were analyzed. This required the addition of

3 schools in the industrial core in the second year to achieve a gradient of air quality that one might expect to show an effect on the child's respiratory health. Financial constraints often dictate that air quality monitoring is done at the same time as the measurements of respiratory disease outcomes in children or in adults. However, without detailed prior information about the distribution of air quality gradients, modification of the design may be required during the course of the study, with the increased difficulty this might give in the analysis of the results. Random selection of schools within each quadrant was performed for this health study in the first year but not with the additional schools in the second year, because all the schools in the industrial core (that is, the area of highest particulate levels) were chosen for inclusion in the study.

The cooperation obtained from the Board of Education for the City of Hamilton and the parents of the children was excellent. We feel that the response rate in excess of 95% obtained in each year enables us to extrapolate any conclusions from the sample chosen to the total population of children at risk.

It was not surprising to find that the

distribution of covariables, which might influence the child's respiratory health, was not uniform across the city. In the examination of the relationship between levels of air pollutants and respiratory health, it is very important that any confounding effect of covariables be distinguished from the effect of air pollution itself. We have shown that the industrial area, which has the highest level of TSP, has also the highest prevalence of domestic smoking, parental respiratory symptoms, and gas cooking (22).

A further important consideration in the study of the effect of air quality on respiratory health is the previous mobility of the sample being studied. As table 4 shows, the proportion of children who had lived at their present address for less than 2 yr varied from 34.4% in the industrial core to 19.0% on the eastern part of the mountain. This difference would also have to be taken into account in any analysis of these results.

Cigarette smoking by the children themselves also becomes important in this particular age group as it can lead to respiratory disease. Tager and coworkers (23) showed that children's smoking habits must be taken into account when looking at any putative effect of parental smoking. Direct validation of the estimates of smoking obtained from our smoking questionnaire was not performed. However, the percentage of children admitting to smoking in the previous 4 wk does increase in the expected direction with increasing age. In addition, these data are comparable to those obtained by Brown and colleagues (24) in their survey of smoking habits in Canadian school children. We are therefore confident that these results do reflect the smoking habits of the children. However, the rate of 4.8% who had smoked in the previous 4 wk is unlikely to affect the interpretation of the results.

TABLE 11  
REPEATABILITY OF LUNG FUNCTION MEASUREMENTS  
RESPIRATORY INFECTIONS EXCLUDED: YEAR 1

Variable	n	Initial		Repeat		t Value	p Value (2-tailed)
		Mean	SD	Mean	SD		
FVC	159	2.02	0.41	2.04	0.41	-3.47	< 0.001
FEV <sub>1</sub>	159	1.66	0.30	1.64	0.30	0.97	0.37
MEF <sub>50</sub>	158	2.26	0.61	2.15	0.58	3.26	0.001
MEF <sub>75</sub>	158	1.00	0.34	0.94	0.32	2.99	0.003
MET	158	0.56	0.17	0.58	0.16	-2.93	0.004
VC	162	2.03	0.40	2.05	0.40	-2.55	0.012
FRC	157	1.17	0.32	1.17	0.29	-0.31	0.76
CVVC	123	0.14	0.08	0.13	0.08	1.33	0.19
N <sub>2</sub> diff	120	1.01	0.59	1.06	0.50	-0.13	0.90

For definition of abbreviations, see tables 7 and 8.

2023379731

The results of a number of quality control procedures were part of the study. The repeatability of the respiratory symptom questions was estimated only when those particular questions were asked from the randomly chosen questionnaires. We thought it important to compute chance-corrected agreement (Kappa), because the raw agreement, when the prevalence of a particular symptom is low, may give a false impression of good agreement, when in fact most of the agreement is due to chance alone. For 3 cases, Kappa could not be computed. On the other hand, by the criterion of Landis and Koch (25), agreement was substantial or better for the questions on asthma, colds to chest, and absence from school for more than 1 wk with a chest illness. It was only slightly less than substantial for the question on wheezing or whistling in the chest.

The ability of young children to perform pulmonary function maneuvers is shown in table 7. The forced expired maneuver was the one most successfully performed. In the older age groups, slow spirometry and the multiple-breath nitrogen washout were equally well performed. In contrast, the single-breath nitrogen washout had a failure rate in excess of 20%. This lack of success for this particular test did not improve in Year 2 and it has been our experience that the single-breath nitrogen washout test is a difficult maneuver to employ in large scale epidemiologic monitoring in children.

In tables 8 and 9, it can be seen that in Years 1 and 2 there were small but significant differences between the initial and repeat estimates of a number of the pulmonary function variables that were not due to the presence of a respiratory infection. The differences were not found to be significant, however, in Year 3. No significant differences were found between the initial and repeat estimates for the variables derived from the multiple- and single-breath nitrogen washout maneuvers. However, for these variables, the coefficient of variation was much greater than for the variables derived from the forced expired maneuver, and therefore the analysis was less powerful in being able to demonstrate a difference if one really existed. An additional measure of association, the correlation coefficient, was high for the variables (FEV<sub>1</sub> and FVC) derived from the forced expired maneuver, but was much less for those variables derived from the single-breath nitrogen washout. This low correlation reduces considerably the usefulness of

the single-breath nitrogen washout test because the amount of random variation may well obscure any true difference between samples.

In conclusion, we have described the design and execution of a study of the effects of environmental factors on the respiratory health of children within a single city. The random selection and high response rate have ensured that the sample is characteristic of the population of interest in the city. The accurate estimation of pollution exposure has required a more comprehensive network of air quality monitors than would normally be employed in a single city. The non-uniform distribution within the city of covariables, such as parental smoking and cough, has implications for the detection of the effects of suspended particulates and SO<sub>2</sub>, especially when those effects are likely to be small at current levels of these pollutants. If present, these effects are only likely to be detected with samples as large as the one that we have studied.

Pulmonary function testing, even in the youngest of children, had a high rate of success with the exception of the single-breath nitrogen washout. We were disappointed with the lower rate of success of this test, its greater degree of variability, and its lack of reproducibility. For these reasons, it was omitted from the Year 3 testing; we feel that its place in large scale epidemiologic testing has not been justified.

#### Acknowledgment

The writers are grateful to the staff of the Urban Air Environment Group, Department of Medicine, for their dedicated work on this project, and to the Hamilton Opinion Research Centre Ltd. for obtaining the questionnaire data.

#### References

- Colley JRT, Douglas JWB, Reid DD. Respiratory disease in young adults: influence of early childhood lower respiratory tract illness, social class, air pollution and smoking. *Br Med J* 1973; 3:195-8.
- Burrows B, Knudson RJ, Lebowitz MD. The relationship of childhood respiratory illness and adult obstructive airway disease. *Am Rev Respir Dis* 1977; 115:751-60.
- Ministry of Environment, Ontario. Hamilton air quality, 1978. Technical Support Section, West Central Region, 1979.
- Lunn JE, Knowelden J, Handyside AJ. Patterns of respiratory illness in Sheffield infant school children. *Br J Prev Soc Med* 1967; 21:7-16.
- Lunn JE, Knowelden J, Roe JW. Patterns of respiratory illness in Sheffield school children; a follow-up study. *Br J Prev Soc Med* 1970; 24:223-8.
- Melia R, Florey C, Swan A. Respiratory illness in British school children and atmospheric smoke and sulphur dioxide, 1973-77: cross-sectional findings. *J Epidemiol Community Health* 1981; 35:161-7.
- Leeder SR, Corkhill RT, Irwig LM, Holland WW, Colley JRT. Influence of family factors on the incidence of lower respiratory illness during first year of life. *Br J Prev Soc Med* 1976; 30:203-12.
- Bland M, Bewley B, Pollard V, Banks MH. Effect of children's and parents' smoking on respiratory symptoms. *Arch Dis Child* 1978; 53:100-5.
- Schilling RS, Letai AD, Hui SL, Beck GJ, Schoenberg JB, Bouhuys A. Lung function, respiratory disease and smoking in families. *Am J Epidemiol* 1977; 106:274-83.
- Lebowitz MD, Burrows B. Respiratory symptoms related to smoking habits of family adults. *Chest* 1976; 69:48-50.
- Colley JR, Holland WW, Corkhill RT. Influence of passive smoking and parental phlegm on pneumonia and bronchitis in early childhood. *Lancet* 1974; 2:1031-5.
- Tager IB, Weiss ST, Munoz A, Rosner B, Speizer FE. Longitudinal study of the effects of maternal smoking on pulmonary function in children. *N Engl J Med* 1983; 309:699-703.
- Ware J, Dockery D, Spiro A, Speizer F, Ferris B. Passive smoking, gas cooking, and respiratory health of children living in 6 cities. *Am Rev Respir Dis* 1984; 129:366-74.
- Melia RJW, Florey CV, Altman DG, Swan AV. Association between gas cooking and respiratory disease in children. *Br Med J* 1977; 2:149-52.
- Keller MD, Lanese RR, Mitchell RJ, Cote RW. Respiratory illness in households using gas and electricity for cooking. II. Symptoms and objective findings. *Environ Res* 1979; 19:504-15.
- Pengelly LD, Kerigan AT, Ballik E, Garside B, Shewchun J. Results of a pilot study on the effect of suspended particulates and sulphur dioxide on the respiratory health of school children. Hamilton, Ontario: Department of Medicine, McMaster University, 1977.
- Epidemiology Standardization Project. *Am Rev Respir Dis* 1978; 118(Part 2):1-120.
- Becklake MR, Soucie J, Gibbs GW, Ghezzo H. Respiratory health status of children in three Quebec urban communities: an epidemiologic study. *Bull Eur Physiopathol Respir* 1978; 14:205-21.
- Mansell A, Bryan C, Levison H. Airway closure in children. *J Appl Physiol* 1972; 33:711-14.
- Brownlee KA. Statistical theory and methodology in science and engineering. 2nd ed. New York: John Wiley and Sons, 1965.
- Nie NH, Hull CH, Jenkins JG, Steinbrenner K, Bent DH, eds. Statistical package for the social sciences. New York: McGraw-Hill, 1975.
- Pengelly LD, Goldsmith CH, Kerigan AT, Inman E. The Hamilton study: distribution of factors confounding the relationship between air quality and respiratory health. *J Air Pollut Control Assoc* 1984; 34:1039-43.
- Tager IB, Weiss ST, Rosner B, Speizer FE. Effect of parental cigarette smoking on the pulmonary function of children. *Am J Epidemiol* 1979; 110:15-26.
- Brown K, Cherry W, Forbes W. Smoking habits of Canadian school children: a summary report, January 1980. Ottawa: Health Promotion Directorate, Health Services and Promotion Branch, Health and Welfare Canada, 1980.
- Landis RJ, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977; 33:159-74.

16

**2023379733**

Strachan, D.P., Elton, R.A. "Relationship Between Respiratory Morbidity in Children and the Home Environment" Family Practice 3: 137-142, 1986.

SUMMARY: The relationships between 12 features of the home environment and respiratory morbidity as reported by parents, and as recorded in general practice records, were studied in 165 children aged seven to eight years. Parental reports of wheeze, nocturnal cough and school absence owing to chest trouble were significantly more common among children with a family history of wheeze, and those from damp or mouldy housing. There were associations between coal fires and nocturnal cough and between an open window and wheeze. Multivariate analyses confirmed these associations to be independent of each other, and of the child's sex and seven other features of the home environment, including gas appliances and parental smoking. These same environmental variables were not consistently related to general practice consultations for wheeze or lower respiratory illness. Damp and mouldy housing, coal fires and open bedroom windows should be investigated further as potentially remediable causes of respiratory disease in childhood.

2023379734

# Relationship Between Respiratory Morbidity in Children and the Home Environment

DAVID P STRACHAN AND ROBERT A ELTON\*

Strachan D P (Department of Community Medicine, University of Edinburgh, Warrender Park Road, Edinburgh EH9 1DW, Scotland) and Elton R A. Relationship between respiratory morbidity in children and the home environment. *Family Practice* 1986, 3: 137-142.

The relationships between 12 features of the home environment and respiratory morbidity as reported by parents, and as recorded in general practice records, were studied in 185 children aged seven to eight years. Parental reports of wheeze, nocturnal cough and school absence owing to chest trouble were significantly more common among children with a family history of wheeze, and those from damp or mouldy housing. There were associations between coal fires and nocturnal cough and between an open window and wheeze. Multivariate analyses confirmed these associations to be independent of each other, and of the child's sex and seven other features of the home environment, including gas appliances and parental smoking. These same environmental variables were not consistently related to general practice consultations for wheeze or lower respiratory illness. Damp and mouldy housing, coal fires and open bedroom windows should be investigated further as potentially remediable causes of respiratory disease in childhood.

The role of environmental factors in the causation of respiratory morbidity in childhood is poorly understood. Hitherto, interest has focussed on the possible hazards of parental smoking and nitrogen dioxide from gas cookers.<sup>1-4</sup> Respiratory illness is more common among children who live in neighbourhoods classified as urban local authority housing,<sup>5</sup> and there is a widespread conviction that housing in some way influences respiratory health.<sup>6</sup> This paper describes an exploratory study of the association between respiratory morbidity and various aspects of the home environment among seven- to eight-year-old children registered with a Scottish urban general practice serving an area of predominantly local authority housing.

## METHOD

In October 1983 a review was made of the general practice records of 198 children born in 1976 and registered with the West Granton Medical Group,

Edinburgh, Scotland. This large practice serves one of the most socially deprived areas of the city. Entries in the records with a mention of wheeze, rhonchi or 'bronchospasm' were termed wheezing episodes, and those with a record of cough, wheeze or breathlessness, or auscultatory signs in the chest, were termed lower respiratory tract illnesses. Coryza, pharyngitis and otitis media were excluded, but an isolated symptom of cough was considered as a lower respiratory illness.

In January 1984 a postal questionnaire was sent to the parents of the same 198 children, enquiring how many nights the child had been kept awake by coughing during the autumn term 1983, and how many days the child had lost from school during the same term owing to chest trouble. These were chosen as readily quantifiable measures of respiratory morbidity that are known to relate to asthma in childhood. The parents were also asked if their child had ever had attacks of wheezing (defined in the questionnaire as breathing making a high-pitched whistling sound) and, if so, whether there had been any attacks over the past two years. This first questionnaire made no reference to interest in the home environment.

Department of Community Medicine, University of Edinburgh, Warrender Park Road, Edinburgh EH9 1DW, Scotland.

\* Medical Computing and Statistics Unit, Medical School, Teviot Place, Edinburgh, Scotland.

In April 1984 a further questionnaire was sent to the same parents enquiring about absence from school owing to chest trouble, and about nocturnal coughing and wheezing during the spring term 1984. Additional questions related to features of the family and home environment which were considered to be possible risk factors for respiratory disease in this age group. Twelve features were expressed as binary variables for analysis:

1. Family history of wheeze: any first degree relative who had ever had attacks of wheezing.
2. Family size of four or more: usually resident at the child's home address.
3. Other children in the family: usual residents under 16 years of age.
4. More than one person per room: usual residents, rooms excluding kitchen and bathroom but including living rooms.
5. Other persons sleeping in the child's bedroom.
6. Child's bedroom unheated: usually, over the past six months (winter 1983-4).
7. Child's bedroom window left open at night: usually, over the past six months (winter 1983-4).
8. Gas: any unvented gas-fired appliance in the house.
9. Coal: any coal-fired appliance in the house.
10. Parental smoking: any person smoking more than five cigarettes per day while in the house.
11. Damp: positive response to the question: is your home affected by damp?
12. Mould: positive response to the question: is your home affected by mould or fungus?

Univariate analysis was by  $2 \times 2$  contingency tables. The cross-product ratio (relative odds) was used to express the degree of association and significance levels were assessed by the chi-square test. Multiple logistic regression analysis was carried out using the GLIM statistical package.<sup>7</sup>

## RESULTS

Complete questionnaire data was received from the parents of 165 (83%) of the children. The response rates were similar for those with and without a record of wheeze in their general practice notes (89% and 81% respectively), suggesting minimal bias, at least with respect to

wheezing. Of these 165 children, 159 (96%) had general practice records complete for the past two years, and 143 (87%) were complete from birth.

### *Risk Factors in the Home*

All but 20 of the 165 children studied lived in local authority housing. Investigation of the associations among the 12 features of the home environment found that damp was significantly more common in homes where coal was burnt ( $\chi^2 = 7.32$ , 1 df,  $P < 0.01$ ), but not in homes using gas ( $\chi^2 = 0.56$ ). No significant association was found between a family history of wheeze and parental smoking or damp housing. Parental smoking was, however, more common in homes affected by damp ( $\chi^2 = 7.36$ ,  $P < 0.01$ ). Of the 50 homes in which damp was reported 66% were also said to have mould or fungus, but only two families reported mould in the absence of damp. The local environmental health department had received complaints of damp or mould from only five of these premises, although in all five cases dampness was confirmed after investigation by the department.

### *Associations with Parental Reports of Symptoms*

The parents of 33 children reported that their child had wheezed at some time. Of these, 31 (94%) were reported to have wheezed during the past two years and 21 (64%) during the spring term 1984. Of these 33 children 22 (67%) had attended their general practitioner at some time with wheeze, but only 16 (48%) had done so in the past two years. Furthermore, a wheezing illness was found in the records of 27 children whose parents reported they had never wheezed. The association of parental reports and general practice records of wheeze was therefore not as strong as might have been expected. The association between general practice consultations for lower respiratory illness and reported respiratory morbidity (school absence and nocturnal cough) was similarly weak.

The associations between parental reports of wheeze and the 12 features of the family and home environment were first assessed by univariate analysis (Table 1). Significant associations were noted with a family history of wheeze, an open bedroom window and damp or mould in the house. Multiple logistic regression analysis including the sex of the child and these 12 features as explanatory variables, with stepwise removal

2023379736



TABLE 1 Degree of association (expressed as relative odds of morbidity) between wheezing, school absence and nocturnal cough and 12 features of the home environment, based on reporting by parents

Risk factor	Prevalence (%)	Ever wheezed (20%) <sup>a</sup>	Autumn term 1983	
			School absence (25%) <sup>a</sup>	Nocturnal cough (49%) <sup>a</sup>
Family history of wheeze	48	2.6*	2.6*	2.8*
Family of 4 or more	82	1.0	0.7	1.0
Other children in family	84	1.1	0.6	0.7
More than one person per room	67	1.0	1.1	0.6
Others sleeping in bedroom	58	1.0	1.1	1.4
Bedroom unheated	60	1.5	1.1	1.6
Bedroom window open at night	28	3.6*	2.2	1.3
Gas appliance	69	0.9	0.8	1.0
Coal appliance	14	0.8	1.1	2.7
Parental smoking	75	2.1	2.9*	1.7
Damp	30	2.7*	3.0**	4.0***
Mould	21	3.9**	2.5*	4.8***

<sup>a</sup> Prevalence

\*P&lt;0.05, \*\*P&lt;0.01, \*\*\*P&lt;0.001

of terms, demonstrated that three factors independently contributed to the risk of wheeze: a family history of wheeze ( $\chi^2=4.35$ ,  $P<0.05$ ), an open bedroom window ( $\chi^2=9.76$ ,  $P<0.01$ ) and mouldy housing ( $\chi^2=9.88$ ,  $P<0.01$ ). Given these factors, an unheated bedroom was of borderline significance ( $0.05<P<0.1$ ).

Absence from school owing to chest trouble during the two terms of the study was reported by the parents of 52 (32%) of the children, with 41 of these absent during the autumn term. Similar associations were found on univariate analysis during each term, suggesting that additional questions about the home environment had not biased the reported morbidity in the second questionnaire. The data relating to the autumn term 1983 are presented in Table 1. A family history of wheeze, parental smoking and damp or mouldy housing emerged as significant risk factors in univariate analysis. Multiple logistic regression analysis, using school absence during either term as the response variable, and the child's sex and the 12 features of the home environment as explanatory variables, demonstrated independent contributions from a family history of wheeze ( $\chi^2=10.39$ ,  $P<0.01$ ) and mould ( $\chi^2=7.04$ ,  $P<0.01$ ). When parental report of wheeze was included as a further explanatory variable, only family history remained as an independent risk factor, whereas the effect of wheeze was highly significant ( $\chi^2=31.4$ ,  $P<0.001$ ).

The parents of 90 (55%) children reported that, at some time during the spring or autumn term, their child had been kept awake by coughing, 81 of these reporting cough during the autumn term. Again, the associations between environmental factors and reported symptoms were similar for each of the two terms in the study. Nocturnal cough during the autumn term was significantly associated with a family history of wheeze and damp and mouldy housing (Table 1). The association with coal-burning was of borderline significance ( $\chi^2=3.6$ ,  $0.05<P<0.1$ ). Multiple logistic regression analysis using nocturnal cough during either term as the response variable, and explanatory variables as before, demonstrated independent contributions from a family history of wheeze ( $\chi^2=9.93$ ,  $P<0.01$ ), coal ( $\chi^2=4.67$ ,  $P<0.05$ ) and mould ( $\chi^2=11.89$ ,  $P<0.001$ ). When wheeze was included as a further explanatory variable, it made an independent contribution ( $\chi^2=11.73$ ,  $P<0.001$ ) but family history, coal and mouldy housing remained significant risk factors for nocturnal cough ( $P<0.05$  in each case).

In the multiple logistic regression analyses reported above, no significant interactions were found between the contributing factors, although with a population of this size, interaction effects would have to be large to reach statistical significance. Thus, the effect of environmental factors did not differ significantly between children with and without a family history of wheeze.

2023379737

TABLE 2 Degree of association (expressed as relative odds of morbidity) between consultations for wheezing illness and lower respiratory illness and 12 features of the home environment, based on general practice records

Risk factor	Prevalence (%)	Wheezing illness		Lower respiratory tract illness	
		Age 0-5 (any) (22%) <sup>a</sup>	Age 5-7 (any) (13%) <sup>a</sup>	Age 0-5 (3 or more) (39%) <sup>a</sup>	Age 5-7 (any) (53%) <sup>a</sup>
Family history of wheeze	48	2.9*	1.4	2.0	0.9
Family of 4 or more	82	3.0	0.5	1.2	1.2
Other children in family	84	1.7	0.6	0.5	1.2
More than one person per room	67	1.0	0.7	1.0	0.7
Others sleeping in bedroom	58	0.7	0.9	0.8	0.9
Bedrooms unheated	60	0.7	1.8	0.7	1.2
Bedroom window open at night	28	1.3	1.9	0.8	1.3
Gas appliance	69	1.8	1.0	0.9	1.2
Coal appliance	14	1.0	3.8	0.4	0.7
Parental smoking	75	3.4*	1.6	1.3	0.8
Damp	30	2.1	1.7	1.2	0.8
Mould	21	2.2	1.5	1.0	1.0

<sup>a</sup> Prevalence\* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ *Associations with General Practice Consultations for Wheezing and Respiratory Illness*

The associations between the 12 features of the family and home environment and general practice consultations for wheezing illness and lower respiratory illness at different ages were assessed by univariate analysis (Table 2). Despite the strong associations of certain environmental features with reported morbidity (Table 1), these same features did not, overall, increase the probability of consultation with respiratory illnesses. When consultations for wheeze during the first five years of life were considered separately, there were significant associations with a family history of wheeze and parental smoking (Table 2). Frequent consultations for lower respiratory illness at ages up to four years did not result in a significantly greater probability of consultation with such an illness at age five to seven years ( $\chi^2 = 3.0$ ,  $0.05 < P < 0.01$ ). These observations would suggest that neither current respiratory morbidity nor long-standing patterns of consultation behaviour have a great influence on consultations for respiratory illness at this age.

The lack of overlap between reports of wheeze by parents and in the general practice records was exploited to investigate whether the association of reported morbidity and the home environment was accounted for by biased symptom reporting (discussed further below). Among the 132 children whose parents denied wheeze, a recorded consultation for wheeze was weakly associated

with parental smoking (odds 3.7,  $\chi^2 = 3.5$ ,  $0.05 < P < 0.1$ ) and damp housing (odds 2.5,  $\chi^2 = 3.1$ ,  $0.05 < P < 0.1$ ), suggesting that the association between symptoms and damp housing may not be entirely due to reporting bias.

## DISCUSSION

Many of the studies relating respiratory morbidity in childhood to environmental factors have relied upon reports of symptoms or diagnoses by parents. Reporting behaviour by parents may not be independent of the environment, particularly when the latter varies with socioeconomic status or is considered by the lay person to be detrimental to health. In a study of adult respondents, 43% of those living in areas of bad housing associated respiratory symptoms with their housing situation, whereas in areas of good housing only 10% did so.<sup>6</sup> Here, general practice records provided an additional data source against which it was hoped to verify parental reports of cough and wheeze. The correlation between reported morbidity and recorded consultations was not as close as might have been anticipated, and the associations which emerged, often at high levels of statistical significance, between the environment and reported symptoms were not found with general practice consultations for wheeze or lower respiratory tract illness.

This raises the possibility that reporting bias may account for some of the associations

2023379738

observed. Parents of symptomatic children may be more aware of potentially adverse environmental circumstances or parents who perceive their housing to be unsatisfactory may report symptoms of a different degree of severity than others. The design of the questionnaire survey to some extent guarded against such bias. The first questionnaire made no mention of interest in the home environment, enquiring only about symptoms. These symptoms were, nevertheless related to environmental variables derived from the second questionnaire. Furthermore, comparison of the responses to each questionnaire did not suggest that inclusion of questions about the home influenced reporting behaviour. Also, if reported data were excluded, damp housing was still associated (albeit at borderline significance) with consultations for wheeze. While it is acknowledged that reporting bias cannot be entirely excluded without objective physiological data, it is considered unlikely that the observed associations are entirely artefactual. Some doubt must be cast on the validity of general practice records as indices of lower respiratory morbidity in this age group.

The population studied was not representative of the city as a whole, but, by concentrating on an area of predominantly local authority housing, possible correlations between housing conditions and socioeconomic status were minimized. Furthermore, a number of other aspects of the home environment which might be expected to vary with social status were controlled in the analysis. In this population, highly significant associations emerged between damp and mould in the house and respiratory morbidity in children, at least as reported by their parents. On the grounds of the strength of the association, its consistency for all measures of reported morbidity studied, and its persistence when a number of possible confounding variables are controlled, damp, mouldy housing deserves consideration as a contributing cause of respiratory disease in children up to seven years old. Damp and mould are a common cause of complaint on aesthetic grounds. These potentially remediable conditions affect an estimated 2.5 million dwellings in the UK<sup>8</sup> and one-quarter of Scottish council houses.<sup>9</sup> The possibility that they might be a hazard to health should be more extensively investigated. In this preliminary enquiry, no independent assessment of damp or mould was made, but future studies could objectively assess both

relative humidity and the presence of fungal moulds or the prevalence of airborne fungal spores.

Others have reported an association between damp bedroom walls and wheeze in adults<sup>10</sup> and a correlation between relative humidity in the bedroom and respiratory symptoms in children.<sup>11</sup> Dampness encourages the growth of house dust mites, but it is unlikely that they are of aetiological significance in more than a few children with mite-sensitive asthma.<sup>12</sup> Most children who wheeze in early childhood eventually develop atopic reactions on skin-tests to common inhaled allergens,<sup>13</sup> and it is possible that fungal spores from mould may react with sensitized bronchi to cause both cough and wheeze. Exercise is a common precipitating cause of wheeze in the asthmatic child, but the available evidence suggests that a damp environment should have a protective effect.<sup>14</sup>

At the age of seven years, however, few children exhibit atopic skin test reactions,<sup>15</sup> and only half of the children with recent wheeze in this study were said to have attacks precipitated by exercise. Most episodes of wheeze in early childhood are thought to be precipitated by infection, and in at least half of cases a virus can be isolated.<sup>15</sup> It has been suggested that high relative humidity may encourage the transmission of viruses in droplet spray.<sup>16</sup>

The association of an open bedroom window with wheeze, but not with school absence or nocturnal cough, raises the possibility that this is a response by parents to the child's symptoms, rather than a factor of aetiological importance. In view of the likelihood that opening the window would raise the relative humidity of the room, such a response may be inappropriate.<sup>11</sup> The association of coal-fired appliances with cough is based on a small number of coal-fired homes but may warrant further consideration.<sup>10,17</sup> Although unvented gas appliances have been associated with respiratory symptoms in some studies of children of this age,<sup>3</sup> the relative risks quoted are small and might not be detected as significant in a study of this size. The data presented here do not support the hypothesis that greater condensation occurs in homes with gas cookers.<sup>4</sup> Parental smoking emerged as a less significant factor than might have been supposed,<sup>12</sup> but the analysis excluded the possibility that either smoking or gas fumes could account for the observed association between damp, mouldy housing and lower respir-

2023379739

atory morbidity in this sample of primary school-children.

#### ACKNOWLEDGEMENTS

Thanks are due to the partners of the West Granton Medical Group for permitting analysis of their records; to Mr A. Turner, Director of Environmental Health, City of Edinburgh Council for information concerning complaints about damp; to Dr M. Fulton for advice throughout the study; and to Prof M. Garraway and Dr I. Grant for comments on an earlier draft of this paper.

#### REFERENCES

- <sup>1</sup> Ware J H, Dockery D W, Spiro A (III), *et al.* Passive smoking, gas cooking and respiratory health of children living in six cities. *Am Rev Respir Dis* 1984; 129: 366-373.
- <sup>2</sup> Charlton A. Children's coughs related to parental smoking. *Br Med J* 1984; 288: 1647-1649.
- <sup>3</sup> Melia R J W, Florey C du V, Chinn S. The relation between respiratory illness in primary schoolchildren and the use of gas for cooking. I: Results from a national survey. *Int J Epidemiol* 1979; 8: 333-338.
- <sup>4</sup> Florey C du V, Melia R J W, Chinn S, *et al.* The relation between respiratory illness in primary schoolchildren and the use of gas for cooking. III: Nitrogen dioxide, respiratory illness and lung function. *Int J Epidemiol* 1979; 8: 347-353.
- <sup>5</sup> Morgan M, Chinn S. ACORN group, social class and child health. *J Epidemiol Community Health* 1983; 31: 196-203.
- <sup>6</sup> McCarthy P, Byrne D, Harrison S, Keithly J. Respiratory conditions: effect of housing and other factors. *J Epidemiol Community Health* 1983; 39: 15-19.
- <sup>7</sup> GLIM Manual. Oxford: Numerical Algorithms Group, 1974.
- <sup>8</sup> Sanders C H, Cornish J P. Dampness: one week's complaints in five local authorities in England and Wales. London: HMSO, 1982.
- <sup>9</sup> Scottish Development Department Building Directorate. Condensation in housing: a report on local authority returns, survey results and remedial measures. Edinburgh: Scottish Office, 1984.
- <sup>10</sup> Burr M L, St Leger A S, Yarnell J W G. Wheezing, dampness and coal fires. *Community Med* 1981; 3: 205-209.
- <sup>11</sup> Melia R J W, Florey C du V, Morris R W, *et al.* Childhood respiratory illness and the home environment. II: Association between respiratory illness and nitrogen dioxide, temperature and relative humidity. *Int J Epidemiol* 1982; 11: 164-169.
- <sup>12</sup> Burr M L, Dean B V, Merrell T G, *et al.* Effects of anti-mite measures on children with mite-sensitive asthma: a controlled trial. *Thorax* 1980; 35: 506-512.
- <sup>13</sup> McNicol K N, Williams H. Spectrum of asthma in children. II: Allergic components. *Br Med J* 1973; 4: 12-16.
- <sup>14</sup> Bar-Or O, Neumann I, Dotan R. Effects of dry and humid climates on exercise-induced asthma in children and pre-adolescents. *J Allergy Clin Immunol* 1977; 60: 163-168.
- <sup>15</sup> Horn M E C, Reed S E, Taylor P. Role of viruses and bacteria in acute wheezy bronchitis in childhood: a study of sputum. *Arch Dis Child* 1979; 54: 587-592.
- <sup>16</sup> Kingdom K H. Relative humidity and air-borne infections. *Am Rev Respir Dis* 1960; 81: 504-512.
- <sup>17</sup> Douglas J W B, Waller R E. Air pollution and respiratory infections in children. *Br J Prev Soc Med* 1966; 20: 1-8.

2023379740

**2023379741**

Anderson, H.R., Bland, J.M., Peckham, C.S. "Risk Factors for Asthma up to 16 Years of Age" Chest 91(6): 127S-130S, 1987.

SUMMARY: From a national cohort of 8,806 children examined at ages seven, 11 and 16 years (National Child Development Study), data on asthma or wheezing illness (AW) were analyzed to describe its natural history in childhood and its risk factors. Factors found to predict the subsequent onset of asthma included male sex of child, mother's age at the child's birth, pneumonia, whooping cough, tonsillectomy/adenoidectomy, allergic rhinitis, eczema and periodic abdominal pain/vomiting attacks. A wide range of perinatal factors, including feeding practices, and social and family factors were shown to have no effect on natural history.

2023379742

## NOTICE

This material may be  
protected by copyright

# Risk Factors for Asthma up to 16 Years of Age\*

## Evidence from a National Cohort Study

H. R. Anderson, M.D.; J. M. Bland, Ph.D.; and  
C. S. Peckham, M.D.

From a national cohort of 8,806 children examined at ages seven, 11 and 16 years (National Child Development Study), data on asthma or wheezing illness (AW) were analyzed to describe its natural history in childhood and its risk factors. Factors found to predict the subsequent onset of asthma included male sex of child, mother's age at the child's birth, pneumonia, whooping cough, tonsillectomy/adenoidec-tomy, allergic rhinitis, eczema and periodic abdominal pain/vomiting attacks. A wide range of perinatal factors, including feeding practices, and social and family factors were shown to have no effect on natural history.

Much of the existing epidemiologic evidence about the etiology of asthma rests on prevalence and follow-up studies and there is a serious lack of population-based cohort data. The National Child Development Study (NCDS) originated in the National Perinatal Study<sup>1</sup> and went on to become a multipurpose cohort study of child development including health. While it was not designed specifically to study the epidemiology of asthma, it is nevertheless possible to obtain valuable information relating to the natural history of asthma. This article describes some of the findings from our analysis of NCDS data which have implications for the etiology of asthma.

### MATERIALS AND METHODS

The NCDS followed-up at ages seven, 11 and 16 all children in England, Scotland and Wales born during one week of March, 1958. At each follow-up, information about current or past asthma or wheezing illness was obtained as part of a structured questionnaire on medical and other topics administered to parents by health visitors. The wording of the asthma questions varied at each interview but it was nevertheless possible to classify subjects at each interview into three categories: no asthma or wheezing; previous asthma or wheezing but not in the past 12 months; and current asthma or wheezing (symptoms reported in the past 12 months). Based on these three possibilities at each of three interviews, 27 mutually exclusive natural history categories can be created. Some of these contain small numbers or are of limited clinical or epidemiologic interest, and so for the purpose of the present analysis a collapsed classification of six natural history categories was used.

These natural history categories were analyzed in relation to medical and social data collected at each of the follow-up medical examinations and home interviews. Factors that have previously been reported to be associated with asthma or wheezing were selected together with those considered likely to influence the natural history of asthma.

The overall association between a variable and the natural history category was tested using the Chi-squared test or one-way analysis of variance as appropriate. Where there was a statistically significant

\*From the Department of Clinical Epidemiology and Social Medicine, St. George's Hospital Medical School, and the Department of Epidemiology, Institute of Child Health, London, England.  
Reprint requests: Dr. Anderson, Clinical Epidemiology and Social Medicine, St. George's Hospital Medical School, Cranmer Terrace, London SW 17 0RE, England.

Law (Title 17 U.S.C. 109)—Lifetime Incidence of Asthma or Wheezing  
(n = 8,806)

Age at interview (yrs)	Asthma or wheezing at any time in past (percent)	
	Cross-sectional	Cumulative*
7	18.3	18.3
11	12.1	21.9
16	11.6	24.7

\*Using information from previous interviews

Table 2—Prevalence of Asthma or Wheezing in  
12 Months Preceding Interview (n = 8,806)

Age at interview (yrs)	Asthma or Wheezing in past 12 months (percent)	
	Cross-sectional	Cumulative*
7	8.3	8.3
11	4.7	10.7
16	3.5	11.1

\*Using information from previous interviews

overall association, the relative risks of each natural history category were calculated. The statistical significance of the relative risk was tested by calculating 95 percent confidence intervals.

### RESULTS

Data on asthma or wheezing were obtained at all three ages for 8,806 of the original NCDS cohort of over 15,000 children living in England, Scotland and Wales and available for follow-up at seven years.

The reported lifetime incidence of asthma or wheezing is shown in Table 1. Using data from all three interviews, a total of 24.7 percent of children had experienced asthma or wheeze by the age of 16 years. When questioned at age 16 years, however, the proportion reporting past asthma or wheeze was less than half this figure (11.6 percent). The prev-

Table 3—Prognosis of Asthma or Wheezing if Current  
(past 12 months) at Age 7 (n = 731)

Persistence of AW and age (yrs)	Percent of 7 year-olds who reported current AW
Current at 11	28.3
Current at 16	16.3
Current at 11 and 16	10.5
Current at 11 or 16	34.1
Not current at 11 or 16	65.9

Table 4—Natural History Categories (n = 8,806)

Category	Percent of sample
Never had asthma or wheezing	75.3
Onset before age 7 but not current at 7 or reported subsequently	8.6
Current at age 7 but not reported subsequently	5.5
Onset age 0 to 7 and also reported at 11 or 16	4.2
Onset age 8 to 11	3.6
Onset age 12 to 16	2.8

Table 5—Factors Predicting the Onset of Asthma or Wheezing

Predictive factors	Overall $\chi^2$ P value	Relative risk of:	Natural history				
			By age 7 not after	At age 7 not after	Age 0-7 and after	Age 8-11 onset	Age 12-16 onset
<b>Perinatal</b>							
Sex of child	<0.001	Boy: girl	1.1	1.2	1.4*	1.3*	1.4*
Mother's age	<0.001	15-19: 20-29 yrs	1.4*	1.5*	1.1	1.9*	1.7*
		15-19: 30+ yrs	1.6*	1.3	1.3	1.9*	2.0*
		20-29: 30+ yrs	1.2	0.9	1.1	1.0	1.2
		Smoker: Non-smoker	1.3*	1.2	0.8	1.0	1.0
Region of child's birth	<0.01	North: Centre	0.7*	0.9	0.9	0.7	1.0
		North: South	0.8*	0.9	1.0	0.9	1.0
		Centre: South	1.1	1.0	1.0	1.2	1.0
<b>Assessed at 7</b>							
History of pneumonia	<0.001	Yes: No	2.0*	2.0*	4.3*	1.5	1.8*
Tonsillectomy/ adenoidectomy	<0.001	Yes: No	1.3*	1.2	1.2	1.2	1.4*
Eczema in 1st year	<0.001	Yes: No	1.2	1.4	5.4*	1.7*	1.5
Eczema after 1st year	<0.001	Yes: No	1.1	1.3	4.7*	1.3	1.7*
Eczema on Dr. exam.	<0.001	Yes: No	0.8	1.1	4.9*	1.6	2.1*
Hayfever or sneezing ever	<0.001	Yes: No	1.3	2.0*	7.1*	1.5	1.7*
Periodic vomiting or bilious attacks ever	<0.001	Yes: No	1.2*	1.4*	1.8*	0.8	1.4*
Periodic abdominal pain ever	<0.001	Yes: No	1.4*	1.3*	1.5*	0.9	1.4*
<b>Assessed at 11</b>							
Whooping cough ever	<0.001	Yes: No	1.2*	1.3*	1.4*	1.4*	1.4*
Eczema in past year	<0.001	Yes: No	1.2	1.2	4.2*	1.9*	1.7*
Hayfever or allergic rhinitis in past year	<0.001	Yes: No	1.0	1.2	5.2	2.2*	1.9*

\*P&lt;0.05.

absence of current asthma was highest at seven years (8.3 percent) but had fallen to 3.5 percent at 16 years (Table 2). At each interview, the lifetime and current rates for the present cohort (those with data available at all interviews) were similar to those among subjects interviewed only once or twice. Of those with current symptoms at seven, 28 percent reported current symptoms at 11 years, 16 percent at 16 years and 11 percent at both ages (Table 3).

For the purpose of analysis, the 27 patterns of questionnaire response were collapsed into the six categories described in Table 4.

From an etiologic standpoint two types of relationship could be discerned. In the first, a given factor was assessed prior to the onset of asthma or wheeze, and could therefore be considered predictive. In the other, the order of occurrence of the factor and the onset of asthma or wheezing could not, from the data available, be shown to be predictive because the assessment of both factors was concurrent. Most factors found to be predictive are shown in Table 5 together with their relative risks. Any concurrent associations for these variables are also shown. Of the perinatal factors the most prominent was sex of the child and the mother's age at birth of the child. Multifactorial analysis was done to explore whether social class or breast feeding might explain this latter relationship, but this was not the case.

Of the factors assessed at seven or 11 years, the main ones predicting subsequent onset of asthma or wheezing were atopic conditions—eczema or allergic rhinitis—and (at

seven years only) periodic vomiting or abdominal pain. A history of pneumonia (at seven years) and whooping cough (at 11 years) were also predictive. Previous tonsillectomy or adenoidectomy reported at age seven years predicted onset in adolescence (though not when reported at 11 years).

Those factors which were concurrently associated with asthma or wheezing but not predictive are shown in Table 6. They mainly comprise upper and lower respiratory conditions but also include fits or convulsions in the first year (but not continuing into later life), enuresis, headaches and one adverse socioeconomic factor—sharing of one or more household facilities.

Those factors not associated with natural history are listed in Table 7. Notably, these included breast feeding, social class and a variety of indicators of socioeconomic circumstances and family stress.

Assessment of smoking in the household was inadequate, available only for the mother while she was pregnant and for both parents when the child was 16 years old. Smoking in pregnancy was associated only with an increased relative risk of asthma or wheezing during the early years of life and smoking by one or both parents reported when the child was 16 years was not related. At 16 years, the child's own smoking habit was unrelated to the presence of asthma or wheezing.

#### DISCUSSION

The National Child Development Study was not designed to examine the etiology of asthma and there are a number of



Table 6—Factors Concurrently Associated with Asthma or Wheezing but not Predictive

Concurrent factors	Overall $\chi^2$ P value	Relative risk of:	Natural history				
			By 7 not after	At 7 not after	0-7 and after	8-11 onset	12-16 onset
Assessed at 7 yrs:							
Household facilities	<0.008	Shared: not shared	1.1	1.5*	0.9	1.0	0.8
Whooping cough ever	<0.001	Yes: No	1.4*	1.2	1.4*	1.2	1.3
Throat/ear infections with fever >3 in past yr	<0.001	Yes: No	1.2	1.6*	1.4*	0.7	1.0
Running ears ever	<0.03	Yes: No	1.3*	1.3	0.9	1.0	1.2
Fits or convulsions in 1st year	<0.001	Yes: No	1.2	1.8*	2.7*	1.0	0.6
Wet by day after 3 yrs	<0.004	Yes: No	1.2	1.7*	1.0	1.5	1.2
Wet by night after 5 yrs	<0.001	Yes: No	1.5*	1.2	1.0	1.2	1.1
Assessed at 11 yrs:							
Household facilities	<0.05	Shared: not shared	1.0	1.4*	1.1	0.8	1.1
Recurrent throat/ear infections in past yr treated by Dr	<0.001	Yes: No	1.1	1.0	1.5*	1.7*	1.1
Discharging ears in past year	<0.07	Yes: No	1.2	1.3	1.8*	1.6	0.7
Tonsils/adenoids removed	<0.001	Yes: No	1.2*	1.3*	1.2	1.2	1.0
Eczema on examination (Dr.)	<0.001	Yes: No	0.8	1.1	4.9*	1.6	2.1*
Recurrent headaches or migraine past year	<0.001	Yes: No	1.2	1.1	1.6*	1.2	1.1
Recurrent vomiting or bilious attacks in past year	<0.09	Yes: No	1.0	1.5*	1.3	1.5	1.0

\*P&lt;0.05

inadequacies in the nature and timing of both the assessment of asthma and wheezing and of etiologic factors. Against this is the advantage that these data relate to a national representative sample and contain a substantial number of subjects followed-up over a long time.

By including all children with reported asthma or wheezing, however mild, the present analysis may have missed associations that relate only to more severe asthma or wheezing, which is the main concern in medical practice. The data do, however, allow a simple grading of severity and this is being analyzed at present.

Considering the logistics of such a national cohort study, the response rate for information about asthma or wheezing on all three occasions of 59 percent of the original NCDS cohort could be judged as successful. Nevertheless, this raises the possibility of bias, which has been examined in detail.<sup>3</sup> It would appear that this is unlikely to have biased our results for relative risks or incidence and prevalence estimates. At any particular age, the prevalence rates among children for whom we had linked data were similar to the rates among those not seen on each occasion. The 12-month prevalence rates observed at age seven years were similar to those of other population surveys which have included all wheezing illnesses.<sup>4,7</sup>

As far as etiology is concerned, the most important findings in this study are those relating to factors which predicted or did not predict the later onset of asthma or wheezing. Among the perinatal factors, a new and possibly important finding was that the risk of all natural history categories apart from persistent asthma or wheezing (reported on all three

occasions) was increased in children of mothers who were under 20 years of age at the birth of the child. This was independent of social class or breast feeding (which were

Table 7—Factors Not Found to Be Predictive or Concurrently Associated with Asthma or Wheezing

<b>Perinatal</b>	
	Birthweight
	Gestational age
	Parity
	Breast/bottle feeding
	Birth order
	Rank in family
	Social class
<b>Assessed at 7</b>	
	Crowding in household
	Number of children in household
	Tenure of accommodation
	Social class
	Separation from mother
	In local authority care
	Absence of one or more biological parents
	Previous measles
<b>Assessed at 11</b>	
	Previous measles
	Social class
<b>Assessed at 16</b>	
	Age at menarche
	Pubic hair rating (boys)
	Smoking of child
	Smoking of parents

unassociated with natural history anyway). Further analysis found that the effect of maternal age existed within the 16 to 19-year-old age group as well. This finding needs to be confirmed by other studies and we can offer no plausible theory to explain it.

The increased risk of asthma or wheezing in boys agrees with other studies,<sup>9</sup> though our results differ from most in that the effect of male sex did not diminish as the age of onset of asthma increased.

The question of whether breast feeding protects against childhood asthma is of great importance since, if true, it would offer insights into etiology and a method of prevention. The evidence is patchy, but a prospective study by Blair<sup>9</sup> found that asthma was more likely to persist in those who were bottle fed. Our results do not confirm this finding, nor was any other effect of infant feeding practice on natural history apparent.

The association between natural history of asthma or wheezing and other atopic conditions confirms the abundant evidence from other prevalence and case-control studies. Additionally, however, we have demonstrated that periodic abdominal pain or vomiting attacks are also predictive and that headaches or migraine are an important concurrent association, though falling just short of significance as a predictive factor. Such associations have also been observed in a separate prevalence study<sup>6</sup> and can no longer be regarded as speculative. We feel that elucidation of the nature of these associations is an important research priority.

The last group of factors found to predict the onset of asthma or wheezing in adolescence were chest infections (pneumonia and whooping cough) and this finding has an important bearing on the question of whether and how early childhood chest troubles may predispose to chronic lung disease in later life as indicated in a previous prospective<sup>10</sup> and retrospective study.<sup>11</sup>

There are various explanations for the associations we have observed. The report of pneumonia or whooping cough may have been a mistaken diagnosis for what was in reality asthma. Chest infection may have led to the later onset of asthma by creating some predisposition which remained latent until adolescence. Both chest infections and asthma may have a common environmental cause or may be the result of a common predisposition via some kind of general "chesty" tendency. Perhaps the asthmatic tendency itself could predispose to chest infections and in some circumstances the chest infection might be expressed prior to the first attack of asthma.

Data about wheezing symptoms and chronic productive cough have been collected from this same cohort at the age of 23 years. Analysis of this additional information should provide further important evidence concerning the origins of both asthma and chronic bronchitis.

## CONCLUSIONS

The National Child Development Study is an important source of nationally representative longitudinal data. While not specifically designed to study asthma, analysis of the data has elucidated a number of factors that predict the subsequent onset of asthma. These include male sex of the child, mother's age at child's birth, pneumonia, whooping cough, tonsillectomy/adenoidectomy, allergic rhinitis, eczema and

periodic abdominal pain/vomiting attacks.

**ACKNOWLEDGMENTS:** We thank Dr. K. Fogelman and his colleagues at the National Children's Bureau for giving us access to the data and Swatee Patel and Nick Tait for helping with the analysis.

## REFERENCES

1. Davie R, Butler N, Goldstein H. From birth to seven. The second report of the National Child Development Study (1958 cohort). London: National Children's Bureau, 1972.
2. Butler NR, Alberman E, eds. Perinatal problems. London: Livingstone, 1969.
3. Fogelman K, ed. Britain's sixteen-year-olds. London: National Children's Bureau, 1976.
4. Williams H, McNicol KN. Prevalence, natural history, and relationship to wheezy bronchitis and asthma in children. An epidemiological study. *Br Med J* 1969; 4:321-25.
5. Burr ML, Eldridge BA, Borysiewicz LK. Peak respiratory flow rates before and after exercise in schoolchildren. *Arch Dis Child* 1974; 49:223-26.
6. Anderson HR, Bailey PA, Cooper JS, Palmer JC, West S. Morbidity and school absence caused by asthma and wheezing illness. *Arch Dis Child* 1983; 58:777-84.
7. Speight ANP, Lee DA, Hey EN. Underdiagnosis and undertreatment of asthma in childhood. *Br Med J* 1983; 286:1253-56.
8. Gregg I. Epidemiological aspects. In: Clark TJH, Godfrey S, eds. *Asthma*, 2nd ed. London: Chapman and Hall, 1983:242.
9. Blair H. Natural history of childhood asthma. 20-year follow-up. *Arch Dis Child* 1977; 52:613-19.
10. Colley JRT, Douglas JWB, Reid DD. Respiratory disease in young adults: influence of early childhood lower respiratory tract illness, social class, air pollution, and smoking. *Br Med J* 1973; ii:195-98.
11. Burrows B, Kaudson RJ, Lebowitz MD. The relationship of childhood respiratory illness to adult obstructive airway disease. *Am Rev Respir Dis* 1977; 115:751-60.

## Occupational Asthma

Moirs Chen-Yung, M.B.,\* and Jean-Luc Melo, M.D.†

This article reviews recent developments in the study of occupational asthma and implications for the overall understanding of asthma. Occupational asthma is a clinical syndrome caused by many different agents. Contribution of studies of experimental inhalation challenge using occupational agents to the knowledge of asthmatic reactions and their mechanisms is discussed. Investigations in the occupational environment into predisposing factors and persistence or recovery after exposure to an allergic agent or nonspecific irritant are reviewed. Approaches to diagnosing asthma in the occupational environment and to assessing functional impairment and disability are outlined. Directions for future research are identified.

Studies in occupational asthma have provided considerable insight into the various etiologic factors, possible pathogenetic mechanism and, to a certain extent, the clinical course of asthma. For the purpose of this presentation, occupational asthma will be defined as asthma caused by a

\*From the Respiratory Division, Department of Medicine, Vancouver General Hospital, University of British Columbia, Vancouver.

†Department of Chest Medicine, Hôpital du Sacré-Coeur, Montreal, Quebec, Canada.

2023379747

Fleming, D.W., Cochi, S.L., Hightower, A.W., Broome, C.V. "Childhood Upper Respiratory Tract Infections: To What Degree Is Incidence Affected by Day-Care Attendance?" Pediatrics 79(1):55-60, 1987.

**ABSTRACT:** Risk factors for acute upper respiratory tract disease in childhood were evaluated in a population-based sample of the Atlanta metropolitan area. Mothers from 449 households containing 575 children less than 5 years of age were selected by random-digit dialing and questioned about upper respiratory tract infection and ear infection occurring in their children during the preceding 2 weeks. Household demographic and socioeconomic characteristics, maternal smoking history and child day-care attendance and breast-feeding information were also obtained. For children less than 5 years of age, the reported incidence of upper respiratory tract infection was 24%, and of ear infection, 6%. Controlling for the other variables measured, day-care attendance was associated with a significantly increased risk of both illnesses. For upper respiratory tract infection, increased risk was present for all children attending daycare ( $P = .02$ , odds ratio = 1.6), whereas for ear infection, risk could be demonstrated only for full-time attendees ( $P = .005$ , odds ratio = 3.8). Maternal smoking was a second independent risk factor for a child's having upper respiratory tract infection (odds ratio = 1.7,  $P = .01$ ). Thirty-one percent of all upper respiratory tract infection among day-care attendees and 66% of all ear infections among full-time day-care attendees were attributable to day-care attendance. Given the proportion of children in day-care, 9% to 14% of the total burden of upper respiratory tract disease in this population was day-care related. As use of child day-care facilities has increased, this specific exposure has become a major factor contributing to transmission of acute upper respiratory tract disease in childhood.

2023379748

## Childhood Upper Respiratory Tract Infections: To What Degree Is Incidence Affected by Day-Care Attendance?

NOTICE  
This material may be  
protected by copyright  
law (Title 17 U.S. Code).

David W. Fleming, MD, Stephen L. Cochi, MD, Allen W. Hightower, MS,  
and Claire V. Broome, MD

From the Meningitis and Special Pathogens Epidemiology Branch and Statistical Services  
Activity, Division of Bacterial Diseases, Centers for Disease Control, Atlanta

**ABSTRACT.** Risk factors for acute upper respiratory tract disease in childhood were evaluated in a population-based sample of the Atlanta metropolitan area. Mothers from 449 households containing 575 children less than 5 years of age were selected by random-digit dialing and questioned about upper respiratory tract infection and ear infection occurring in their children during the preceding 2 weeks. Household demographic and socioeconomic characteristics, maternal smoking history and child day-care attendance and breast-feeding information were also obtained. For children less than 5 years of age, the reported incidence of upper respiratory tract infection was 24%, and of ear infection, 6%. Controlling for the other variables measured, day-care attendance was associated with a significantly increased risk of both illnesses. For upper respiratory tract infection, increased risk was present for all children attending day care ( $P = .02$ , odds ratio = 1.6), whereas for ear infection, risk could be demonstrated only for full-time attendees ( $P = .005$ , odds ratio = 3.8). Maternal smoking was a second independent risk factor for a child's having upper respiratory tract infection (odds ratio = 1.7,  $P = .01$ ). Thirty-one percent of all upper respiratory tract infection among day-care attendees and 66% of all ear infections among full-time day-care attendees were attributable to day-care attendance. Given the proportion of children in day care, 9% to 14% of the total burden of upper respiratory tract disease in this population was day care related. As use of child day-care facilities has increased, this specific exposure has become a major factor contributing to transmission of acute upper respiratory tract disease in childhood. *Pediatrics* 1987;79:55-60; upper respiratory tract infection, day-care attendance.

these illnesses, including acute upper respiratory tract infection and otitis media, may occasionally progress to more severe disease, most often they are self-limited. Despite their relatively benign nature, however, upper respiratory tract infectious illnesses are important causes of childhood morbidity, and their treatment consumes a substantial portion of available health care resources.<sup>1</sup>

During the past decade, it has been demonstrated that risk of a number of childhood infections, including hepatitis,<sup>2</sup> diarrheal diseases,<sup>3</sup> and invasive *Haemophilus influenzae*,<sup>4</sup> is increased by day-care attendance. During this same time, the number of children younger than 5 years of age in the United States who are enrolled in day care has undergone a dramatic increase.<sup>5</sup> Although several studies have suggested that the risk of upper respiratory tract disease may be increased for some day-care attendees,<sup>6-8</sup> the importance of this association has not been well defined.

In this study, we examined risk factors for acquisition of infections of the upper respiratory system in children less than 5 years of age and specifically evaluated the role played by day-care attendance. Using population-based data, we determined the amount of illness attributable to this increasingly common childhood exposure.

### METHODS

A cross section of all households containing children less than 5 years of age in Atlanta was surveyed by telephone from mid-July through mid-September 1984.

### Sampling Procedure

Telephone numbers consisting of prefixes serving the study area and four randomly selected final

Infections of the upper respiratory system are the most common illnesses affecting children less than 5 years of age in the developed world. Although

Received for publication Feb 18, 1986; accepted May 28, 1986.  
Reprint requests to (D.W.F.) Centers for Disease Control, Division of Bacterial Diseases, Atlanta, GA 30333.  
PEDIATRICS (ISSN 0031-4005). Copyright © 1987 by the American Academy of Pediatrics.

digits were generated by computer. Every possible telephone number in the seven counties composing the metropolitan area (population 1.9 million) had an equal likelihood of being selected and called; no call-clustering techniques were used. Each number selected was called at least twice during business hours and at least six times during evenings and weekends before being discarded. Only households with children less than 5 years of age were enrolled.

#### Questionnaire Administration

Using a standardized questionnaire, trained interviewers obtained informed consent and then collected information from the guardian of the children in the household, preferably the mother. Data obtained included household demographic and socioeconomic characteristics, current maternal smoking history, and current breast-feeding and day-care attendance information for all children less than 5 years of age. All children within a given household were enrolled to ensure that our sample accurately represented all children in the study area with respect to household size and other related characteristics. A 15% sample of completed questionnaires was validated with a follow-up telephone call; no child's illness or day-care status was reclassified as a result of these calls.

#### Definitions

History of recent acute respiratory infection (cough, cold, or ear infection) was obtained directly from the child's guardian.<sup>6,7,9</sup> Because independent physician confirmation of illness was not required, we have used the term "ear infection" rather than otitis media to denote parental reported cases of infections of the ear. Criteria including antibiotic administration and physician visit were used if respondents needed clarification. We did not attempt to identify specific etiologic agents. Incidence of disease rather than duration of symptoms was assessed. To limit interviewer and respondent bias, illness history was elicited before parents were asked about day-care attendance. Children were considered case children if they had been ill with upper respiratory tract infection or ear infection at any time during the 2 weeks before the interview was conducted. Day care was defined as regular (>4 h/wk) supervised care of at least two unrelated children. Each child's day-care status was determined individually, based on enrollment at the time of interview. Part-time enrollment was defined as five to 39 hours' attendance per week and full-time as 40 or more hours per week.

#### Analysis

Two analyses of risk factors were undertaken;

one for children reported to have upper respiratory tract infection and the other for children reported to have ear infection. An automatic interaction detection program was used to assist in selection of variables for inclusion in an unconditional logistic regression model. Only associations that were biologically plausible were considered. We did not attempt to analyze or control for transmission of illness within households because we could not distinguish between primary and secondary cases. The number of children younger than 5 years in the household, a variable included in the model, may serve as a surrogate for intrafamilial spread. Final models were obtained by first putting all candidate variables into the model and then eliminating any variable that was not significant and whose elimination did not alter the odds ratio estimates of significant variables by more than 15%. Etiologic fractions among exposed groups (EF<sub>e</sub>) were calculated by the formula:  $EF_e = (\text{probability of disease in exposed} - \text{probability of disease in unexposed}) / (\text{probability of disease in exposed})$  and were standardized for the entire population by weighting the values from individual strata according to the percentage of the population represented by that strata. The disease probabilities used were those determined by the regression model.

#### RESULTS

A total of 3,952 households in the study area were surveyed. Of these, 3,387 contained no children younger than 5 years, 78 were unwilling to answer whether children were present and 487 contained at least one young child. Of these latter households, complete interviews were obtained for 449 (92%). Twenty-six percent of households (118) contained more than one child, and information regarding illness was collected for 575 children.

#### Upper Respiratory Tract Infection

Twenty-four percent of the children surveyed (139/575) were reported to have had an upper respiratory tract infection during the 2 weeks before the interview. The incidence of reported illness was divided equally by sex with 24% of both boys (75/307) and girls (64/268) affected. Race did not appear to be a significant risk factor; illness was reported for 23% of white children (96/421), 27% of black children (40/146), and 40% of children of other races (4/10). The frequency of upper respiratory tract infection did vary somewhat with age; incidence in children younger than 36 months was 27% (91/338), and in children 36 months or older, 20% (47/232).

On univariate analysis, children who attended

day-care facilities appeared to be more likely than children who did not attend to have had symptoms of an upper respiratory tract infection during the 2 weeks preceding the interview (32% [55/175] of attendees *v* 21% [84/400] of nonattendees;  $P = .01$ ,  $\chi^2$ ). A significant difference in risk between part-time and full-time attendance could not be demonstrated, although there was a suggestive trend in children younger than 36 months (42% [23/55] incidence in full-time attendees *v* 28% [11/39] in part-time attendees,  $P = .2$ , Fisher exact test). The type of day-care facility, ie, residential *v* nonresidential, and the length of time the child had been attending were not statistically associated with the likelihood of upper respiratory tract infection.

The association of day-care attendance with upper respiratory tract infection was further evaluated by logistic regression in a model that contained other variables considered to be possible risk factors for disease. These variables included family income, crowding (dichotomized at less than *v* equal to or more than one person per room), and number of children less than 5 years of age, maternal smoking, and child's race and age (dichotomized at 36 months). Current breast-feeding was included as a possible protective factor in children less than 6 months of age.

In this model, children who attended day care were significantly more likely than children who did not attend to have had a parent-reported upper respiratory tract infection during the 2 weeks before interview (odds ratio = 1.6,  $P = .02$ , Fig 1). In addition to day-care attendance, a second factor, maternal smoking, was also associated with increased risk of upper respiratory tract infection (odds ratio = 1.7,  $P = .01$ ). The effects of day-care attendance and maternal smoking were independent of one another. Child's age, although itself not

a risk factor (odds ratio = 1.2,  $P = .4$ ), did significantly modify the effect of a third variable, household crowding. Living in crowded conditions was significantly associated with upper respiratory tract infection in children younger than 36 months (odds ratio = 2.4,  $P = .02$ ) but not in children 36 months or older (odds ratio = 0.6,  $P = .4$ ). No statistically significant association with risk of upper respiratory tract infection was seen for family income, number of children less than 5 years, and child's race, and no protective benefit of breast-feeding could be demonstrated (Table 1).

Clustering of illnesses within households did not seem to significantly affect the association of upper respiratory tract infection with day-care attendance. This relationship in households with only one child less than 5 years of age was similar to that in households with two ill children (odds ratio = 1.73 *v* 1.72), and the prevalence of day-care attendance in ill children from households containing no other children less than 5 years was similar to that observed in children from households with another ill sibling (41% [35/85] *v* 40% [12/30]).

#### Ear Infection

Six percent (34/575) of children less than 5 years of age were reported to have had an ear infection during the 2 weeks before the interview. Ear infection was reported more often for boys than girls (7.2% *v* 4.5%), but this difference was not statistically significant. Black children and white children were affected equally (6.1%); none of the ten children of other races were reported ill. Compared with upper respiratory tract infection, the incidence of ear infection was more influenced by age. Incidence was 8.6% (29/337) in children 0 to 35 months of age and 2.1% (5/233) in children 3 or 4 years of age. Children with ear infection were significantly more likely than children without ear infection to have had upper respiratory tract infection symptoms during the preceding 2 weeks (65% [22/34] *v* 22% [116/535]; odds ratio = 6,  $P < .001$ , Fisher exact test).

Univariate analysis suggested that, as with upper respiratory tract infection, children attending day

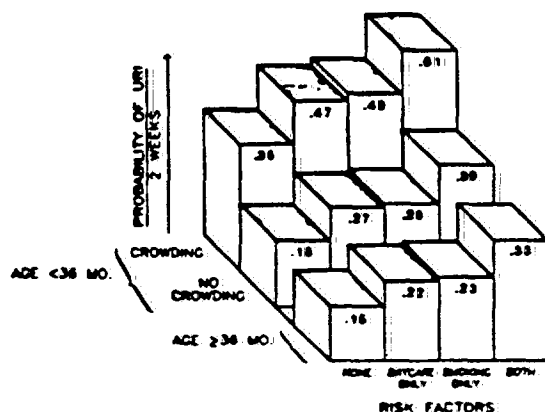


Fig 1. Probability of upper respiratory tract infection according to age, crowding, maternal smoking, and day-care status.

TABLE 1. Variables Not Included in Final Upper Respiratory Tract Infection Model

Variable	Odds Ratio (Point Estimate)	P Value
No. of children <5 yr	0.7	.17
Race	1.1	.76
Breast-feeding	1.0	.98
Income (\$)		
0-19,999	1.0	
10-34,999	1.5	.14
≥35,000	1.0	.91

care were at increased risk for development of ear infection. For ear infection, however, only children who attended a day-care facility 40 or more hours per week could be shown to be at increased risk. This association with full-time attendance was present when either all children or only children younger than 36 months were evaluated (Table 2). Although the number of children with ear infection who attended day-care full time was relatively small, the type of day-care facility, ie, residential v nonresidential, and the length of time the child had been attending did not appear to be associated with increased risk of disease.

The association between full-time day-care attendance and ear infection was evaluated in a logistic regression model containing the same variables that were used for the upper respiratory tract infection analysis. Concomitant upper respiratory tract infection was not considered as a separate risk factor because this illness may, in many instances, represent an intermediate step between exposure to a risk factor and ear infection.<sup>8,10</sup> Clustering of ear infections within a household occurred only once and, thus, was not a factor in analysis. In the ear infection model, full-time day-care attendance was strongly associated with increased risk of ear infection (odds ratio = 3.2,  $P = .005$ ). Age was a second important predictor of disease, with children younger than 36 months at higher risk than children 36 months of age or older (odds ratio = 3.3,  $P = .02$ ). Among young children, as with upper respiratory tract infection, crowding was an important factor predicting disease (odds ratio = 3.4,  $P = .01$ ); in the older age group, data were insufficient to assess the effect of this variable (Fig 2). For ear infection, family income, number of children less than 5 years of age, maternal smoking, and child's race and breast-feeding status were not significantly associated with risk (Table 3). Two factors, maternal smoking and part-time day-care attendance, which were associated with the risk of upper respiratory tract infection, were not associated with the risk of ear infection. This finding may be due to the smaller numbers of children with ear infections and consequent lack of statistical power or

TABLE 2. Incidence of Ear Infection by Day-Care Attendance Status for All Children and Children 0 to 35 Months of Age

Day-Care Attendance Status	Incidence of Ear Infection (%)	
	All Children	0-35 Mo
Nonattendees	4.8 (19/395)	7.0 (17/244)
Part-time attendees	4.1 (3/73)	5.3 (2/38)
Full-time attendees	11.7 (12/102)	18.2 (10/55)
Status not available	(0/5)	(0/1)
Total	5.9 (34/575)	8.7 (29/338)

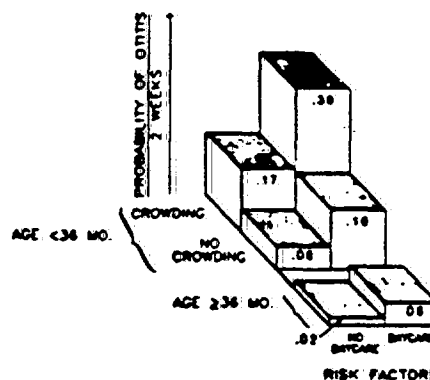


Fig 2. Probability of ear infection according to age, crowding, and day-care status.

TABLE 3. Variables Not Included in Final Ear Infection Model

Variable	Odds Ratio (Point Estimate)	P Value
No. of children <5 yr	0.7	.43
Maternal smoking	1.1	.82
Race	1.0	.93
Breast-feeding	1.9	.32
Income (\$)		
0-19,999	1.0	
20-34,999	0.9	.87
≥35,000	0.8	.73

alternatively to actual differences in risk factors for these two syndromes.

#### Attributable Risk

Perhaps the most meaningful measure of the amount of upper respiratory tract disease associated with day-care attendance is the etiologic fraction among the exposed children or  $EFe_{(day-care)}$ , which can be interpreted as the proportion of respiratory illness among children who attend day care that is directly related ("attributable") to this exposure.

In this study, the  $EFe_{(day-care)}$  for upper respiratory tract infection, adjusted for the other variables shown to be associated with upper respiratory tract infection, was 31%. Thus, approximately one third of upper respiratory tract infections in children who attend day care may be attributable to this specific exposure. The  $EFe_{(day-care)}$  for upper respiratory tract infections varied slightly by age and was 30% for children younger than 36 months and 33% for children 36 months of age or older.

For ear infections, the  $EFe_{(full-time day-care)}$  was 66%, standardized for the other variables shown to be associated with ear infection, and thus approximately two thirds of ear infection contracted by full-time day-care attendees may be directly re-



**TABLE 4.** Etiologic Fraction Among Exposed Groups ( $EFe_{\text{day-care}}$ ) and Population Attributable Risk of Upper Respiratory Tract Infection and Ear Infection Associated with Day-Care Attendance

Child's Infection and Age (Mo)	$EFe_{\text{day-care}}$	Children Attending Day-Care (%)	Population Attributable Risk (%)
Upper respiratory tract			
0-35	.30	29	9
≥36	.33	34	11
Ear infection			
0-35	.64	16	10
≥36	.68	20	14

lated to that specific exposure. The age-specific  $EFe_{\text{(all-time day-care)}}$  for ear infection was 64% for children 0 to 35-months of age, those at highest risk, and 68% for children 3 and 4 years of age.

The amount of upper respiratory tract disease in all young children that is directly related to day-care attendance (the etiologic fraction among the population, also called the population attributable risk) depends not only on the proportion of illness related to attendance but also on the proportion of children who attend. This latter figure is likely to depend on a variety of factors including geographic region, season of the year, and age of the children involved. In Atlanta, during the summer of 1984, the population attributable risk for day-care attendance varied between 9% and 11% for upper respiratory tract infection and between 10% and 14% for ear infection, depending on child's age (Table 4).

## DISCUSSION

Although more than 11 million children in the United States attend some form of day care,<sup>11</sup> estimates of risk have not been available for many of the illnesses to which these children are exposed, and the need for population-based studies has become increasingly apparent.<sup>11,12</sup> In particular, although the association between day-care attendance and infections of the upper respiratory system was suggested more than 35 years ago,<sup>13</sup> the contribution of day-care exposure to overall risk for these diseases has not been defined.

This study was designed to quantify the relation between day-care attendance and risk of childhood upper respiratory tract infections. Controlling for the effect of other risk factors, children in this cohort who were enrolled in day care were substantially more likely to have both upper respiratory tract infection and ear infection. Because these children were randomly selected from the general population, we could calculate that approximately

one third of upper respiratory tract infections among day-care attendees and two thirds of ear infections among full-time day-care attendees were directly related to attendance. Because data regarding the proportion of children in the population attending day-care facilities were also available, we were able to estimate that 9% to 14% of all upper respiratory tract infections and ear infections in children less than 5 years of age may occur as a result of day-care attendance, a figure generalizable to other areas to the extent that day-care attendance patterns in Atlanta are similar to attendance patterns elsewhere. These estimates provide a useful assessment of the influence of day-care attendance on the overall risk of upper respiratory tract infection in young children. Respiratory illness results in an estimated 17.4 million physician visits a year in the United States<sup>1</sup> and for otitis media alone, an estimated annual expenditure of more than \$2 billion.<sup>14</sup>

These percentages should be interpreted with appropriate caution. Having a child in day care may alter the likelihood that parents will notice and report illness in their children. This study determined a point estimate of risk based on parental reporting of illness during a 2-week period and, as such, should be viewed as only a first step in quantifying the effect of day-care attendance on the incidence of childhood upper respiratory tract infections. Nevertheless, the case definition based on parental reporting can be partially validated by the results of the analysis. If parents were reporting respiratory infections when no illness had occurred, one would not expect to find significant associations with crowding or maternal smoking. The substantial portion of upper respiratory tract infection linked to day-care attendance in this study suggests that it would be useful to determine whether specific etiologic agents may be particularly associated with this risk.

Additional studies that assess risk over season should be undertaken. For example, the risk of upper respiratory tract infection associated with day-care attendance calculated by this study may be a minimum estimate; day-care attendance may be more strongly linked with disease during the winter respiratory illness season when the likelihood of the introduction of upper respiratory tract infection into a day-care facility may be greater. Alternatively, a greater background incidence of viral infection during the winter might reduce the added risk associated with day-care attendance.

Several aspects of analysis other than the relation between upper respiratory tract illness and day-care attendance deserve comment. The similarity of the risk factor models for upper respiratory tract

2023379753

infection and ear infection demonstrates the close association between these two illnesses and reaffirms the likely role of upper respiratory tract infections in the pathogenesis of ear infection.<sup>8,10</sup> The data regarding maternal smoking underscore the link between passive exposure to smoke and development of upper respiratory tract infection in children.<sup>12,16</sup> In this study, the proportion of upper respiratory tract infections in children of smoking mothers attributable to this exposure (84%) and the total population attributable risk (10%) were comparable to those calculated for day-care attendance.

As risk factors, however, there is a major difference between maternal smoking and day-care attendance. Whereas maternal smoking is totally preventable, day-care attendance is not. This difference highlights an increasingly obvious dilemma: child day care provides an irreplaceable service; yet, by its nature, it also results in enhanced transmission of infectious illnesses. The most practical approach to this problem—reduction of risk among those children who attend—rests on the assumption that differences in day-care facilities and children's exposures within those facilities may affect degree of risk. For diarrheal disease, this assumption seems warranted; risk has been shown to be influenced by a variety of specific day-care characteristics.<sup>9</sup> Whether the same is true for respiratory disease remains an open question. Identification of specific factors that are associated with increased risk of upper respiratory tract disease within day-care facilities should be a primary goal of future study.

#### ACKNOWLEDGMENTS

We thank our telephone interviewers, Patricia Adams, Lela Baughman, Unice Davis, Suzanne Gaventa, and

Rubina Mamdani and the support provided by the Office of Epidemiology, Georgia Department of Human Resources.

#### REFERENCES

1. Cypress BK: Patterns of Ambulatory Care in Pediatrics: The National Ambulatory Medical Care Survey, data from the national health survey, series 13, No. 75, Department of Health and Human Services publication No. (PHS) 84-1736. Government Printing Office, 1983.
2. Hadler SC, Webster HM, Erben JJ, et al: Hepatitis A in day-care centers: A community-wide assessment. *N Engl J Med* 1980;302:1222-1227
3. Sullivan P, Woodward WE, Pickering LK, et al: Longitudinal study of occurrence of diarrheal disease in day care centers. *Am J Public Health* 1984;74:987-991
4. Isre GR, Conner JS, Broome CV, et al: Risk factors for primary invasive *Haemophilus influenzae* disease: Increased risk from day care attendance and school-aged household members. *J Pediatr* 1985;106:190-195
5. Marwick C, Simmons K: Changing childhood disease pattern linked with day-care boom. *JAMA* 1984;251:1245-1251
6. Strangert K: Respiratory illness in preschool children with different forms of day care. *Pediatrics* 1976;57:191-196
7. Strangert K: Otitis media in young children in different types of day-care. *Scand J Infect Dis* 1977;9:119-123
8. Henderson FW, Collier AM, Sanyal MA, et al: A longitudinal study of respiratory viruses and bacteria in the etiology of acute otitis media with effusion. *N Engl J Med* 1982;306:1377-1383
9. Doyle AB: Incidence of illness in early group and family day-care. *Pediatrics* 1976;57:607-612
10. Giebink GS: The pathogenesis of pneumococcal otitis media in chinchillas and the efficacy of vaccination in prophylaxis. *Rev Infect Dis* 1981;3:342-352
11. The Child Day Care Infectious Disease Study Group: Public health considerations of infectious disease in child day care centers. *J Pediatr* 1984;105:683-701
12. Goodman RA, Osterholm MT, Granoff DM, et al: Infectious diseases and child day care. *Pediatrics* 1984;74:134-139
13. Hoeselvik L: Respiratory infections among children in day nurseries. *Acta Paediatr Scand* 1949;37(suppl 74):1-103
14. Bluestone CD: Otitis media in children: To treat or not to treat? *N Engl J Med* 1982;306:1399-1404
15. Pedreira FA, Guandolo VL, Feroli EJ, et al: Involuntary smoking and incidence of respiratory illness during the first year of life. *Pediatrics* 1985;75:594-597
16. Bonham GS, Wilson RW: Children's health in families with cigarette smokers. *Am J Public Health* 1981;71:290-293

2023379755

Martin, C.J., Platt, S.D., Hunt, S.M. "Housing conditions and ill health" British Medical Journal 294:1125-1127, 1987.

**ABSTRACT:** Lack of empirical evidence that living in damp houses has detrimental effects on health may partly be due to inadequate research. A preliminary study was therefore carried out of a random sample of council owned residences in a deprived area of Edinburgh, a respondent from consenting households being interviewed to obtain a profile of the physical and mental health of all adults and children. In addition, information was gathered about other factors that might be important, particularly smoking and selective bias in the allocation of tenants to houses. Independent measures of dampness were made by environmental health officers.

No conclusive effects of damp on the health of adults were identified. Nevertheless, children living in damp houses, especially where fungal mould was present, had higher rates of respiratory symptoms, which were unrelated to smoking in the household, and higher rates of symptoms of infection and stress.

Housing should remain an important public health issue, and the effects of damp warrant further investigation.

2023379756

## Housing conditions and ill health

CLAUDIA J MARTIN, STEPHEN D PLATT, SONJA M HUNT

### Abstract

Lack of empirical evidence that living in damp houses has detrimental effects on health may partly be due to inadequate research. A preliminary study was therefore carried out of a random sample of council owned residences in a deprived area of Edinburgh, a respondent from consenting households being interviewed to obtain a profile of the physical and mental health of all adults and children. In addition, information was gathered about other factors that might be important, particularly smoking and selective bias in the allocation of tenants to houses. Independent measures of dampness were made by environmental health officers.

No conclusive effects of damp on the health of adults were identified. Nevertheless, children living in damp houses, especially where fungal mould was present, had higher rates of respiratory symptoms, which were unrelated to smoking in the household, and higher rates of symptoms of infection and stress.

Housing should remain an important public health issue, and the effects of damp warrant further investigation.

### Introduction

The *BMJ* argued recently that the health implications of poverty, unemployment, and inadequate housing were not being emphasised strongly enough and made a plea for the formation of a public health alliance to highlight these issues.<sup>1</sup> Certainly, the role of housing conditions in the aetiology of illness appears to have received comparatively little attention since the decline of tuberculosis in the 1950s.

Most recent studies of housing conditions have concentrated on the relation between living in a damp house and respiratory complaints such as asthma<sup>2</sup> and wheeze.<sup>3,4</sup> Rising and penetrating damp provide the moist conditions conducive to germination of spores of mould fungi. Fungal spores, in turn, are believed to affect the respiratory tract by producing lesions in tissue, by forming saprophytic colonies on plugs of mucus, and by acting as allergens causing rhinitis, alveolitis, and asthma.<sup>5,6</sup> Some studies have suggested that ambient humidity influences the viability of viruses in droplet sprays.<sup>7,8</sup> The association between damp housing and health problems, however, is not clear cut, possibly being complicated by other factors known to affect health, such as smoking and poverty. A further serious flaw has been that the presence of damp has been reported by the householder or by the research team, casting doubt on the objectivity of the findings because of either the tenant's desire to get rehoused or bias in the experimenter.

This study was carried out in response to the concern of residents in a deprived area of Edinburgh about the possible effects of damp on their health. The preliminary study aimed at investigating the relation between damp housing and the physical and mental health of tenants and their children.

Edinburgh city is ringed by estates of council housing of varying quality and desirability, and the study area is regarded as one of the less (but by no means least) desirable in which to live (K Brown, unpublished master's dissertation, 1986). The area consists of

Research Unit in Health and Behavioural Change, University of Edinburgh, Edinburgh EH1 2QZ

CLAUDIA J MARTIN, MA, PhD, research fellow

SONJA M HUNT, MA, PhD, senior research fellow

MRC Unit for Epidemiological Studies in Psychiatry, Royal Edinburgh Hospital, Edinburgh EH10 5HF

STEPHEN D PLATT, MSc, PhD, research sociologist

Correspondence to: Dr Martin.

2023379757

mainly residential flats, constructed in the 1930s and 1960s, situated close to the Forth on low lying land exposed to winds.

## Method

In order to overcome problems of this in respondents or experimenter bias in reporting damp Edinburgh District Council's environmental health department agreed that an independent survey of dwellings would be carried out by environmental health officers. Assessments of damp and health were not linked until the data collection was complete, because the study was double blind. The housing department made records available from which a random one in four sample of tenanted dwellings was drawn from the study area, which comprised one postcode sector of Edinburgh and contained just over 2000 dwellings. A duplicate list of the sample was given to the environmental health department for its own survey.

A questionnaire was drawn up and used in a pilot study in an area similar to that under investigation. The questionnaire focused on sociodemographic data, reports of symptoms and use of health services for all household members, smoking, household income, and heating type and cost. A standardised measure of perceived health problems, the Nottingham health profile,<sup>12</sup> was also included. At the end of the interview schedule the tenants' permission was also included. At the end of the interview schedule the tenants' permission was also included.

Between March and May 1986 a team of experienced interviewers visited each household to interview a woman if possible, or a man if no woman was available. They were instructed to interview a woman if possible, as women tend to have more knowledge of the health problems of the family as a whole. During the same period the survey of sample dwellings was conducted by environmental health officers using protocols, which measure relative humidity and damp. This was supplemented by observation. For most analyses a composite measure of damp was derived from these measures whereby any sign of damp—that is, damp, condensation, or mould—was regarded as evidence of a "damp house." It was not feasible from the information available to rate each house on a measure of severity of dampness.

Except where stated otherwise, all comparisons between damp and non-damp households were carried out by  $\chi^2$  test or Mann-Whitney U test. The significance level was set at 0.05, though we recognise that where multiple comparisons are made one in 20 may be significant by chance.

## Results

A total of 358 interviews were completed, representing a response rate of 73%. The refusal rate was 12%, and 15% of the sample could not be contacted. Environmental health officers obtained information for 300 of these households. There were no differences in any of the main sociodemographic variables between those households for which we had full information and the 58 for which we did not. A total of 294 (82%) of the respondents were women. The age range was 19-91, 143 (49%) were aged under 45 and 150 (51%) aged over 45, which was representative of the community as a whole. Unemployment was high, at slightly fewer than half (45%) of the whole. Employment was below pensionable age there was no household where the respondent was below pensionable age there was no adult in paid employment. A third of all households were receiving supplementary benefit.

According to the independent assessments 73 (24%) of the dwellings were damp, 51 (17%) of the total, 70% of the damp dwellings had fungal mould.

Children's health in the previous two months. Except where stated otherwise figures are numbers (percentages) of children

	Damp houses (n=35)	Non-damp houses (n=45)
Median No of symptoms (range)	3 (0-8)	2 (0-10)*
Non-respiratory symptoms:		
Cough and phlegm	9 (27)	5 (11)*
Cold/flu	11 (33)	12 (28)
Wheezing	16 (30)	12 (28)
Nervous	7 (21)	3 (7)*
Tiredness	2 (6)	6 (14)
Headache	3 (9)	17 (38)
Itchy	8 (24)	11 (25)
Fever/temperature		
Respiratory symptoms:		
Persistent cough	16 (46)	24 (55)
Wheezing	15 (43)	19 (43)
Short breath	18 (53)	27 (60)
Sore throat	4 (12)	8 (18)
Sneezing	22 (63)	41 (90)*
Any respiratory symptoms		

\* $p<0.01$ .

The proportion of houses identified as damp, however, varied considerably by street. Almost 80% of the damp houses were concentrated in nine of the 26 streets surveyed. Most of the damp dwellings were built between 1930 and 1936.

More damp houses were overcrowded than dry ones (4 (11%) v 9 (43%);  $p<0.05$ ). Tenants in damp houses were significantly younger ( $p<0.001$ ) and more likely ( $p<0.05$ ) to have children. In households with children, however, the number of children was similar in those that were damp (median 2, range 1-4) and non-damp (median 2, range 1-4). A greater proportion of respondents in damp houses had moved to their current homes because of previous poor housing (79 (40%) v 59 (26%);  $p<0.05$ ). There were no differences between damp and non-damp households in respect of the duration of tenancy (47 (65%) v 157 (69%) tenants had lived in their present homes for five or more years); tenants having moved to their present homes for health reasons (10 (44%) v 23 (10%)); weekly household income (58 (79%) v 186 (82%) had a net weekly household income of less than £100); whether Color gas fires were used for heating (15 (21%) v 41 (18%)); or whether Color gas fires were used for heating (15 (21%) v 41 (18%)); or whether Color gas fires were used for heating (15 (21%) v 41 (18%)).

## HEALTH OF RESPONDENTS

The study sample as a whole appeared to be characterised by very poor health. During the previous two months 255 (85%) of the respondents reported at least one symptom or health problem (124 (41%) concerning respiratory symptoms such as persistent cough, wheeze, or blocked nose), 120 (40%) had consulted their general practitioner, and two thirds had taken a prescribed or non-prescribed medicine; 164 (56%) reported long term or recurrent health problems. There were, however, no significant differences between those living in damp and non-damp houses.

Nottingham health profile scores were generally high for the six areas of perceived problems (sleep, energy, pain, physical mobility, emotional reactions, and social support) suggesting raised levels of distress. The only significant difference, however, was for emotional reaction scores, which were higher for those in damp houses ( $p<0.05$ ).

## HEALTH OF CHILDREN

The table shows that defective housing was strongly associated with ill health among children, a third of whom were living in houses considered to be damp. The number of symptoms was higher in the damp houses ( $p<0.01$ ) and there were significant differences for several symptoms: colds and phlegm, diarrhoea, "nervous," and headache. Though there were no significant differences in individual respiratory symptoms, children in damp houses were significantly more likely to have had at least one respiratory problem in the past two months ( $p<0.01$ ).

Log linear analysis<sup>13</sup> was performed in order to rule out the possibility that the difference in incidence of respiratory problems was introduced by the confounding effects of smoking and the presence of other children in the household. Cigarette smoking was not found to be associated with the respiratory symptoms in children, but the more children living in the household the greater was the likelihood of such symptoms. More importantly, after controlling for number of children and smoking a significant main effect for dampness remained. There were no interactions between the main effect for dampness and smoking, nor for associations between the use of Color gas and respiratory symptoms in children.

In a further analysis we compared children in "mouldy" ( $n=24$ ) and "non-mouldy" ( $n=77$ ) dwellings. In general, children in houses where mould was found had the higher symptom rates. Moreover, in addition to the significant associations listed in the table, rates of wheezing and sore throat were significantly higher in homes affected by mould than in other homes (10 (42%) v 12 (16%);  $p<0.01$ ; and 16 (67%) v 29 (33%);  $p<0.05$ ). In an attempt to explore the possibility of reporting bias (see below) we also examined the relation between the tenant's perception of whether or not the house was damp and reported symptoms. There were no significant differences for any symptom in either children or adults.

## Discussion

This study found no clear evidence to support the hypothesis that damp housing has a detrimental effect on the physical health of adults; nevertheless, there was evidence that those living in damp houses had more emotional distress. The principal finding, however, was of significant associations between living in a damp and, more specifically, "mouldy" house and ill health among children. Not

20233379758

only respiratory problems but other symptoms suggestive of infections and stress were more common in children in damp dwellings.

Respiratory problems may be due to the fact that the spores of many fungi act as allergens, sensitising mucous membranes and producing symptoms of wheezing, cough, fever, and general malaise in both atopic and non-atopic people. Vomiting and diarrhoea in children in damp houses are harder to explain. Nevertheless, if mycotoxins in fungi were ingested their metabolites might give rise to the symptoms. It seems probable that headache and "nerves" in the children may partly be related to the other symptoms or be a response to tension in the home; equally, however, they may be symptoms of emotional upset, possibly associated with recurrent symptoms, disruption of school and social activities, and the living conditions themselves.

Several studies have suggested an association between poor housing and health problems. Acceptance of these findings and action on them, however, have been conspicuously absent, explanations including the financial and political implications of improving housing. At the scientific level most studies have been criticised on the grounds that the relation of ill health to poor housing could be confounded by other variables, such as low income, smoking, type of heating, overcrowding, housing allocation policies, and bias of experimenters or respondents, or both. This study, though based on fairly small numbers, has addressed such criticisms. It is plainly impossible to allow for all confounding factors; however, several alternative explanations of our findings appear to be unlikely.

Firstly, the sample was homogeneous with respect to social class and income. More than three quarters of respondents or their partners, or both, actually in employment were in manual occupations. Virtually all the households were on low incomes, and there were no income differences between those in damp and non-damp houses.

Secondly, the results show that certain aspects of the respondents' behaviour were not implicated. In particular, smoking made no contribution to children's respiratory symptoms. This is at variance with other studies, "but our sample was drawn from a social group with high rates of smoking," and the adverse effects of parental smoking on children are largely confined to children under the age of 1 year. Overcrowding and the number of children in the household were not contaminating factors; even after controlling for these factors significant effects for dampness remained. The use of Calor gas fires in the home was not associated with either dampness or children's respiratory symptoms. Indeed, that the damp houses were mostly confined to particular streets makes it unlikely that the tenants themselves created the conditions which gave rise to damp.

Thirdly, issues of self selection and bias in the allocation of tenants to dwellings must be addressed—that is, that the "sick" may be more likely to move into poor housing or be allocated the worst properties. For the most part council tenants have little choice about where they will live and, though the low desirability of the study area inevitably leads to some self selection, it is by no means the least desirable of the council housing schemes in and around Edinburgh. Families living in damp houses were more likely to have come from poor conditions, but they were not more likely to have moved for health reasons. It was children, not adults, with poor health who were more likely to be living in damp houses; there was no evidence that behaviour problems in children were a factor in the allocation of families to particular houses. The only clear selection bias operating appeared to be of the infirm elderly being allocated better housing. There were no significant differences between damp and non-damp households in the length of time tenants had lived in their homes, and most had lived in the same house for more than five years.

As in most surveys, information about respondents' and children's health was reported by the respondent. Physical examination of all household members was beyond the scope of this study. Inevitably this raises questions about the possibility of reporting bias. Differential overreporting by those in damp houses would be manifested in respondents' reports of their own as well as their children's health, but it was clear that health differences were confined to children. Perhaps even more importantly, respondents who reported their homes to be damp were not more likely to report symptoms

either in themselves or in their children. The possibility of experimenter or respondent bias was minimised by having an independent survey of damp and not comparing data on dampness and health until the health data were coded.

Though it might be suggested that smokers may underreport symptoms such as coughing or wheezing, this was not the case in our study, where the highest rates of respiratory symptoms were found in heavy smokers. This, in turn, suggests that children's respiratory symptoms were not being underreported. Finally, there was no association between the respondents' mental state and the reporting of physical symptoms in children, suggesting that "psychologically distressed" mothers were not overreporting health problems in their children.

This study considered obvious confounding factors which might explain the findings and has gone a long way to ruling out selection and reporting biases. The findings appear to be robust and the association between living in a damp house and ill health in children cannot easily be attributed to other factors. Clearly, the number of households studied was fairly small and a larger investigation, using the same double blind methodology, is warranted and is being planned. If our findings are replicated the public health implications will require urgent consideration. Improvements in the health of the population in the past 100 years have largely been a consequence of improved living conditions and thus a healthier home environment. The early exposure to an adverse living environment is likely to increase vulnerability to illness in later life—particularly to the chronic respiratory diseases, which are still a main cause of morbidity and mortality in Britain.

This study was supported by grants from Edinburgh District Council, the Scottish Home and Health Department, and the Scottish Health Education Group. We are grateful to the departments of environmental health and housing for their cooperation. We also thank the following for their advice and comments at different stages of research: Jane Jones, Lyn Jones, Steve Engleman, Shirley Platz, Martin Donaghy, Mike Porter, Mel Birtley, and David McQueen.

## References

- Smith R. The need for a public health alliance. *Br Med J* 1986;293:344-7.
- Todd S. Danger: a health risk. *Community Action* 1984;24:7-9.
- Melis RJW, Florry CDV, Morris RW, et al. Childhood respiratory illness and the home environment. II: association between respiratory illness and nitrogen dioxide, temperature and relative humidity. *Int J Epidemiol* 1982;11:164-9.
- Burr ML, St Lager AS, Yarnall JWG. Wheezing, dampness and coal fires. *Community Med* 1981;3:205-9.
- Bassett H. Moulds in allergy. *Journal of Allergy Research* 1978;15:151-4.
- Macneil K. Sensitization risk from inhalation of fungal spores. *J Laryngol Otol* 1954;68:765-75.
- Kingdom KH. Relative humidity and air-borne infections. *Am Rev Respir Dis* 1960;81:504-12.
- Buckhead FE, Tyrrell DAJ. Loss of infectivity on drying various viruses. *Nature* 1962;195:1063-4.
- Bloch MT, Holman MJ, Darg EF, et al. Stability of airborne rhinovirus type 2 under atmospheric and physiological conditions. *Abstracts of the Annual Meeting of the American Society of Microbiology* 1976;38:193.
- Hunt SM, McEwen J, McKenna SP. *Measuring health status*. London: Croom Helm, 1986.
- Baker RJ, Nelder JA. *The GLIM system (release 3) manual*. Oxford: Numerical Algorithms Group, 1978.
- Lacey J, Papp J, Cross T. Anticoccidial and fungus spores in air in respiratory allergens. In: Shapiro DA, Board RG, eds. *Safety in microbiology*. London: Academic Press, 1972:151-84.
- Saito M, Enomoto M, Umada M, et al. Field survey of mycotoxin-producing fungi contaminating human foodstuffs in Japan: II biological effects of the mycotoxins produced by the fungi isolated from foodstuffs. In: Purchart IFH, ed. *Symposium on mycotoxins in human health*. London: South African Medical Research Council, Macmillan, 1971:43-78.
- McCarthy P, Byrne D, Harrison S, Keithley J. Respiratory conditions: effect of housing and other factors. *J Epidemiol Community Health* 1985;39:15-9.
- Serlach DP, Elton RA. Relationship between respiratory morbidity in children and the home environment. *Family Practice* 1986;3:137-42.
- Byrne DS, Harrison SP, Keithley J, McCarthy P. *Housing and health: the relationship between housing conditions and the health of council tenants*. Aldershot: Gower Publishing, 1986.
- Colley JRT. Respiratory symptoms in children and parental smoking and phlegm production. *Br Med J* 1974;ii:201-4.
- Blund M, Brewley BR, Pollard V, Banks MH. Effect of children's and parents' smoking on respiratory symptoms. *Arch Dis Child* 1978;53:100-5.
- Marrs A, Matheson J. *Smoking attitudes and behaviour*. London: HMSO, 1983.
- Ferguson DM, Horwood LJ, Shannon FT, Taylor B. Perinatal smoking and lower respiratory illness in the first three years of life. *J Epidemiol Community Health* 1981;35:180-4.
- McKewen T, Lave CR. *An introduction to social medicine*. Oxford: Blackwell, 1974.
- Holmes RW, Halli T, Bennett AE, Elliot A. Factors influencing the onset of chronic respiratory disease. *Br Med J* 1969;ii:205-8.

(Accepted 10 March 1987)

2023379759





Koo, L.C., Ho, J.H.C., Matsuki, H., Shimizu, H., Mori, T., Tominaga, S. "A Comparison of the Prevalence of Respiratory Illnesses among NonSmoking Mothers and Their Children in Japan and Hong Kong" American Review of Respiratory Disease 138:290-295, 1988.

SUMMARY: Previous epidemiologic studies have associated symptoms of chronic bronchitis and other respiratory diseases with the risk for lung cancer. To assess the possible precursor or premonitory role of these conditions for lung cancer among nonsmokers, a comparison of the prevalence rates of these conditions in 2 urban industrialized communities (Hong Kong and a Tokyo suburb) with a 300% difference in female lung cancer incidence rates was conducted. A community survey of 314 nonsmoking mothers and their children in Hong Kong, and 243 mothers and children in Japan showed that the prevalence of reported chronic cough and sputum symptoms was 10 or more times higher in Hong Kong than in Japan. The disparity in the rates of respiratory diseases/symptoms was most apparent in the comparison of children. Occupational exposure to dust or fumes and larger household sizes were found to be associated with higher levels of respiratory illnesses among the Hong Kong mothers. The much higher prevalence rates of respiratory symptoms among Hong Kong than among Japanese subjects correlated with each community's female lung cancer incidence rates of 27.1 versus 8.1/100,000, respectively.

2023379761

# A Comparison of the Prevalence of Respiratory Illnesses among Nonsmoking Mothers and Their Children in Japan and Hong Kong<sup>1,2</sup>

LINDA C. KOO, JOHN H.-C. HO, HIDEAKI MATSUKI, HIROYUKI SHIMIZU, TORU MORI, and SUKETAMI TOMINAGA

## Introduction

A previous study on lung cancer among Hong Kong Chinese females found that patients with lung cancer were more likely to report a previous history of chronic cough or phlegm expectoration than were age-matched control subjects (1). These results were applied to those who had ever or never smoked, and a dose-response relationship was found between increasing years of experiencing these symptoms and risk for lung cancer.

The association of a previous history of respiratory diseases such as chronic bronchitis and pneumonia with lung cancer was first reported by Doll and Hill in their 1952 study on the etiology of lung cancer (2). Subsequently, other studies (3-5) also reported this association, although most did not segregate the effects of a past history of active smoking and the occurrence of these diseases.

Because Hong Kong Chinese females tend to have notably high lung cancer incidence rates, with a 1982 world age-adjusted incidence rate of 27.1 per 100,000 (6), a comparative study of females from a low incidence area such as Japan, with a world age-adjusted incidence rate of only 8.1 per 100,000 (7) for 1975-1979 in the Kanagawa Prefecture, might shed some light on this possible etiologic association. Both societies are racially similar and share a predominantly urban, industrialized environment. Yet their cultural habits and diets are sufficiently different to raise the possibility that their respective exposures to a variety of pollutants or protectors account at least in part for the 300% difference in their lung cancer rates.

The purpose of this cross-sectional study was to compare the prevalence rates of respiratory illnesses among children and mothers residing in 2 communities, one in Japan and the other in Hong Kong. Only subjects with no previous his-

**SUMMARY** Previous epidemiologic studies have associated symptoms of chronic bronchitis and other respiratory diseases with the risk for lung cancer. To assess the possible precursor or premontory role of these conditions for lung cancer among nonsmokers, a comparison of the prevalence rates of these conditions in 2 urban industrialized communities (Hong Kong and a Tokyo suburb) with a 300% difference in female lung cancer incidence rates was conducted. A community survey of 314 nonsmoking mothers and their children in Hong Kong, and 243 mothers and children in Japan showed that the prevalence of reported chronic cough and sputum symptoms was 10 or more times higher in Hong Kong than in Japan. The disparity in the rates of respiratory diseases/symptoms was most apparent in the comparison of children. Occupational exposure to dust or fumes and larger household sizes were found to be associated with higher levels of respiratory illnesses among the Hong Kong mothers. The much higher prevalence rates of respiratory symptoms among Hong Kong than among Japanese subjects correlated with each community's female lung cancer incidence rates of 27.1 versus 8.1/100,000, respectively. *AM REV RESPIR DIS* 1988; 138:290-296

tory of active smoking were included. We wanted to know if differences found in their respective prevalence rates of respiratory illnesses would help explain the differing lung cancer incidence rates in the 2 populations. In addition, we wanted to know if these data could point to possible precursor respiratory conditions that might increase the individual's susceptibility to environmental carcinogens or that might indicate early premonitory symptoms since lung cancer is usually detected decades later.

## Methods

### Japanese Subjects

In July 1982, students from Grades 2 through 6 attending 2 public primary schools around the Tokyo area were surveyed. One school was located at the Sugunami-ward in Tokyo and the other in Aikawa in the Kanagawa Prefecture, which is located about 50 kilometers west of Tokyo. The mothers of the surveyed children were also studied. These subjects were chosen from these districts because they would be representative of Japanese living in urban and rural environments in Japan. The Sugunami-ward is a typical urban residential area with several heavily traveled roads traversing the district. The Aikawa area is characteristically rural without major factories and heavily traveled roads.

The response rate was 99.6% for the 457

children and 88.2% for their 403 mothers/guardians. Out of this sample, the following data were not included in this analysis: incompletely answered questionnaires ( $n = 38$ ), guardians who were not mothers of the children ( $n = 11$ ), any who reported a previous history of active smoking ( $n = 68$ ), and, in situations where 2 or more children from the same family were surveyed and attended the same school ( $n = 95$ ), only 1 of the children was randomly selected. Thus, the results from 243 mother-child pairs were analyzed for this study.

### Hong Kong Subjects

A government-subsidized primary school in the Ngau Tau Kok area of the Kwun Tong

(Received in original form April 7, 1987 and in revised form February 5, 1988)

<sup>1</sup> From the Departments of Community Medicine and of Surgery, Medical Faculty, University of Hong Kong, Hong Kong; the Department of Public Health, Tokai University School of Medicine, Isehara, Kanagawa Prefecture; the Department of Public Health, Tohoku University School of Medicine, Sendai; the Division of Epidemiology, Research Institute of Tuberculosis, Japan Anti-tuberculosis Association, Tokyo; and the Aichi Cancer Center, Research Institute, Chikusa-ku, Nagoya, Japan.

<sup>2</sup> Supported by Monbusho International Scientific Research Program and the Hong Kong Anti-Cancer Society.

TABLE 1  
AGE DISTRIBUTION AMONG MOTHERS

Age (yr)	Hong Kong		Japan	
	(n)	(%)	(n)	(%)
< 30	18	5.7	13	5.4
31-35	99	31.5	79	33.1
36-40	123	39.2	87	36.4
41-45	39	12.4	49	20.5
46-50	27	8.6	10	4.2
> 51	8	2.5	1	0.4
Unknown			4	
Total	314		243	
Mean age*	37.8		39.3	

\* *t* test, *p* value = 0.412.

district of Hong Kong was selected in cooperation with the local government's Department of Education to represent subjects from a working class neighborhood. The site is surrounded by public housing in high-rise buildings and by small stores, and is within a few blocks of the small- and medium-sized factories that are common in this district.

Initially, 2 classes from each grade of 2 to 6 were planned for the study since each class averaged 36 students, and these numbers would approximate the age and sex distribution of the Japanese subjects. However, after data collection began, it was realized that some students in different classes were siblings, so an additional class in Grade 4 was included in the study. Thus, a total of 11 classes, i.e., 390 children and mothers were contacted for the study. The response rate for the return of the questionnaire was 100% for the children and 97% for their mothers/guardian (11 did not return the questionnaire). Using the same inclusion criteria as those for the Japanese subjects, 314 mother-child pairs were included in this analysis. To simulate the summer weather conditions of the Japanese collection time, the survey was conducted from May 20 to 30, 1985. The mean temperature and humidity in Hong Kong during the data collection period was 27° C and 81% humidity. The same data for Tokyo during July 1982 was 22° C and 77%, respectively. The Hong Kong data were collected in late May instead of July because the students would be off for summer vacations and thus not accessible.

#### Data Collection Forms

A modified version of the questionnaires originally developed by the American Thoracic Society Division of Lung Disease (ATS-DLD) (8) and the British Medical Research Council (BMRC) (9) to survey the prevalence of respiratory diseases was used. Questions were asked on the occurrence of the following: chronic cough or phlegm of ≥ 3 months duration (to eliminate those associated with acute upper respiratory tract infections), bronchitis, pneumonia, asthma, tuberculosis, allergic rhinitis, and other chest diseases.

The version for the children also included

TABLE 2  
AGE DISTRIBUTION AMONG CHILDREN

Age (yr)	Hong Kong		Japan	
	(n)	(%)	(n)	(%)
6	0		11	4.5
7	10	3.2	44	18.1
8	46	14.6	20	8.2
9	54	17.2	45	18.5
10	80	25.5	29	11.9
11	48	15.3	82	33.7
12	67	21.3	12	4.9
13	9	2.9	—	
Total	314		243	
Mean age*	10.1		9.4	
Girls, %†		48		46

\* *t* test, *p* value = 0.0001.† *t* test, *p* value = 0.588.

questions on sources and amounts of passive smoking exposure, and whether the child participated in home cooking activities. These questionnaires were distributed to the children at school and taken home with instructions that it be answered for the child by the mother or female guardian.

The version for the mothers included more detailed questions on cooking activities, active smoking history, and exposure to dust or fumes in the workplace. These questionnaires were distributed to the children at school with instructions that they should take them home for their mothers to fill out.

#### Data Analysis

The data collected in the questionnaires were coded and then processed by computer using the SPSS-X statistical package. Because the questionnaire asked about respiratory symptoms (i.e., cough, sputum, wheezing) and respiratory diseases (i.e., pneumonia, allergic rhinitis, bronchitis, asthma, tuberculosis), both were covered under the term "respiratory illnesses." These terms are distinguished

in this study because "respiratory symptoms" is a lay term that is easier for the subjects to identify with, whereas "respiratory diseases" would mean that a physician had diagnosed such a condition.

Analysis of the data included descriptive, comparative, and analytical work. In comparing the results between subjects from Hong Kong versus those from Japan, *t* tests or chi-square tests were usually done to estimate the statistical significance of the findings. Analysis on the relationship of multiple illnesses per person and various exposure categories utilized Pearson's goodness of fit test. A test for linear trend in the proportions was done when dose-response relationships were suggested (10). To statistically assess the risk among the exposed group versus the unexposed group, the following were calculated: relative risks as the ratio of these 2 proportions, attributable risk as the percentage of the overall risk in the exposed group, and the population-attributable risk as the difference in risk among the whole population (which we assume the entire sample represented) and the risk in the unexposed group (10).

#### Results

The age distribution of the 314 Hong Kong Chinese mothers and 243 Japanese mothers is shown in table 1. The Hong Kong Chinese mothers tended to be slightly younger, with a mean age of 37.8 versus 39.3 yr among the Japanese mothers, but these differences were not statistically different (*t* test, *p* value = 0.41). On the other hand, the 314 Hong Kong school children were slightly older than their Japanese counterparts (table 2), with the mean age of the former being 10.1 yr and that for the latter being 9.4 yr, which was statistically significant (*t* test, *p* value = 0.0001). The sex ratio for the children was not significantly

TABLE 3  
PREVALENCE OF SELF-REPORTED RESPIRATORY ILLNESSES AMONG NON-SMOKING MOTHERS

Respiratory Symptom/Disease	Prevalence (%)		Chi-Square <i>p</i> Value
	Hong Kong ( <i>n</i> = 314)	Japan ( <i>n</i> = 243)	
Chronic cough ≥ 3 months, %	5.7	0.4	0.006
Chronic phlegm ≥ 3 months, %	8.0	0.4	0.0000
Cough and phlegm ≥ 3 months, %	3.2	0.4	0.0197
Cough or phlegm ≥ 3 months, %	10.5	0.4	0.0026
Bronchitis, %	7.6	5.8	0.3823
Ever had pneumonia, %	1.0	2.9	0.0897
Ever had asthma, %	1.3	2.9	0.1785
Ever had tuberculosis, %	1.6	2.1	0.6817
Ever had allergic rhinitis, %	11.5	12.4	0.7498
Ever had other chest diseases, %	0.3	1.2	0.2041
≥ 1 of the above chest illnesses, %	24.8	20.9	0.7054
Chest illnesses per sick mother, mean <i>n</i>	1.49	1.29	0.137*

\* *p* value by *t* test.

TABLE 4  
PREVALENCE OF RESPIRATORY ILLNESSES AMONG CHILDREN  
AS REPORTED BY THEIR MOTHERS

Respiratory Symptom/Disease	Prevalence (%)		Chi-Square p Value
	Hong Kong (n = 314)	Japan (n = 243)	
Cough > 3 months, %	7.0	0.4	0.0001
Phlegm > 3 months, %	9.2	0.4	0.0000
Cough and phlegm, %	3.5	0	—
Cough or phlegm, %	12.8	0.8	0.0000
Cough or phlegm, yr/person	4.7	3.5	0.742*
Wheezing > 3 months, %	7.6	1.7	0.0013
Wheezing, yr/person	4.8	6.8	0.180*
Ever had allergic rhinitis, %	9.2	11.1	0.4654
Ever had pneumonia, %	8.0	0	—
Ever had asthma, %	8.3	10.7	0.3304
> 1 of the above chest illnesses, %	25.2	18.7	0.066
Chest illnesses per sick child, mean $\pm$ SD	1.96	1.31	0.0001*

\* p value by t test

TABLE 6  
RELATIONSHIP BETWEEN THE FREQUENCY  
OF RESPIRATORY ILLNESSES BETWEEN  
MOTHER/CHILD IN HONG KONG  
AND IN JAPAN\*

Illnesses per Child (n)	Illnesses per Mother (n)		
	0	1+	Total
<b>Hong Kong</b>			
0	186	48	234
1+	49	30	79
Total	235	78	313
Relative risk = 1.85†			
<b>Japan</b>			
0	157	33	190
1+	28	15	43
Total	185	48	233
Relative risk = 2.00‡			

\* The presence of the following respiratory illnesses unrelated to cold/flu: cough > 3 months; phlegm > 3 months; wheezing; pneumonia; asthma; allergic rhinitis; bronchitis; TB; and other chest diseases.

† Pearson's correlation coefficient, 0.18; p value = 0.009.

‡ Pearson's correlation coefficient, 0.17; p value = 0.005.

different for the 2 groups, with 48% of the Hong Kong children and 46% of the Japanese children being girls (t test, p value = 0.59).

The prevalence rates among mothers reporting a previous history of respiratory illnesses is shown in table 3. Among Chinese mothers, 5.7% (n = 18) reported a previous history of chronic cough, and 8.0% (n = 25), a history of chronic phlegm expectoration lasting 3 or more months. This contrasted with only 1 Japanese mother (0.4%) who reported having both such symptoms. For the other respiratory diseases, the prevalence rates between the 2 groups did not reach statistical significance (p < 0.05). In general, there was a tendency for more Hong Kong mothers to report a previous history of chest problems (24.8 versus 20.9%); among those who had such diseases, Hong Kong mothers had more illnesses per person (1.49 versus 1.29) than did Japanese mothers. There was no relationship between the prevalence rates of respiratory illnesses and age of the mother in either population (chi-square, p value = 0.236 for Hong Kong mothers and 0.274 for Japanese mothers).

The prevalence of respiratory illnesses among children was similar to that of their mothers (table 4). One (0.4%) Japanese child was reported by the mother to be suffering from chronic cough, and another (0.4%) was reported to have chronic phlegm, whereas among the Hong Kong children these percentages were 7.0% (n = 22) and 9.2% (n = 29), respectively. When the 2 symptoms were combined, 12.8% (n = 40) of the Hong Kong children had one or both symptoms, whereas this was true for only 0.8% (n = 2) of

the Japanese children. All of these differences were statistically significant.

Among the other respiratory illnesses for the children, those in Hong Kong had statistically higher frequencies of wheezing (7.6 versus 1.7%) and pneumonia (8.0 versus 0%) than did their Japanese counterparts. The reported rates for allergic rhinitis and asthma were not statistically different for the 2 groups.

In the summary measurements, 25.2% of the Hong Kong children had one or more of the surveyed respiratory illnesses versus 18.7% among the Japanese children (p = 0.066). Moreover, among those with such illnesses, the former group had a significantly larger mean number of problems per child (1.96) than did the latter (1.31).

The distribution of multiple illnesses within a single individual in the 2 areas is shown in table 5. Hong Kong mothers

and children consistently had higher percentages of such individuals than did the Japanese. This discrepancy was most apparent among the children, with 24 Hong Kong children (7.7%) having 3 or more respiratory illnesses versus only 1 Japanese child (0.4%) with such a history, and a comparison of their mean number of illnesses per child was highly significant (p = 0.0001).

The frequency of illnesses in the mothers was related to that reported for their children as shown in table 6. In both populations, mothers who reported one or more respiratory illnesses for themselves were about twice as likely to report such illnesses in their children. Pearson's goodness of fit test showed this relationship to be highly significant.

TABLE 5  
FREQUENCY OF MULTIPLE RESPIRATORY ILLNESSES AMONG MOTHERS AND  
CHILDREN IN HONG KONG AND JAPAN

Illnesses per Mother† (n)	Hong Kong Mothers		Japanese Mothers		Illnesses per Child† (n)	Hong Kong Children		Japanese Children	
	(n)	(%)	(n)	(%)		(n)	(%)	(n)	(%)
0	235	75.1	185	79.4	0	234	74.8	190	81.5
1	54	17.3	39	16.7	1	45	14.4	30	12.9
2	14	4.5	4	1.7	2	10	3.2	12	5.2
3	7	2.2	5	2.1	3	11	3.5	1	0.4
4+	3	0.9	—	—	4+	13	4.2	—	—
Total	313	100	233	99.9‡		313	100.1‡	233	100
Mean	0.37		0.27			0.69		0.24	

\* The presence of the following respiratory illnesses unrelated to cold/flu: cough > 3 months; phlegm > 3 months; pneumonia; allergic rhinitis; bronchitis; asthma; TB; and other chest diseases.

† The presence of the following respiratory illnesses unrelated to cold/flu: cough > 3 months; phlegm > 3 months; wheezing; pneumonia; asthma; allergic rhinitis.

‡ Due to rounding off, the total sum was not 100%.

TABLE 7  
RELATIONSHIP OF OCCUPATIONAL DUST OR GAS/FUME EXPOSURE WITH  
RESPIRATORY ILLNESSES AMONG HONG KONG MOTHERS\*

Exposure at Work	Total Number of Mothers	Mothers with $\geq 1$ Respiratory Illnesses†		
		(n)	(%)	Relative Risk
Dust				
No exposure	246	55	22.4	1.00
Mild	39	12	30.8	1.38
Moderate	25	9	36.0	1.61
Severe	4	2	50.0	2.23
Total exposed	68	23	33.8	1.51
Gas				
No exposure	278	63	22.7	1.00
Mild	23	9	39.1	1.72
Moderate	11	5	45.5	2.00
Severe	2	1	50.0	2.20
Total exposed	36	15	41.7	1.84

\* Linear trend p value  $< 0.05$ ; Pearson's correlation coefficient significance p value presence and absence of illnesses: dust = 0.017, gas = 0.007. Exact number of illnesses: dust = 0.007, gas = 0.0008.

† The presence of the following respiratory illnesses unrelated to cold/flu: cough  $\geq 3$  months, phlegm  $\geq 3$  months, pneumonia, allergic rhinitis, bronchitis, asthma, TB, and other chest diseases.

TABLE 8  
COMPARATIVE PROFILES OF HONG KONG AND JAPANESE  
MOTHERS AND CHILDREN

Lifestyle Variable	Hong Kong		Japan		Chi-Square p Value
	(n)	(mean)	(n)	(mean)	
Mother currently works outside the home	106	33.9%	68	28.0%	0.136
Father currently smokes	110	35.6%	146	60.1%	0.0000
Home has ventilated cooking*	251	79.9%	192	79.2%	0.789
Mean household size	314	5.31	243	4.54	0.000†

\* Cooking area has electric ventilating fan or cooking hood.

† p value by t test.

To understand the role of occupational exposures, the Hong Kong mothers were asked in the questionnaire whether they had ever worked for a year or more in places where they were exposed to noticeable levels of dust/smoke or gases/fumes, the degree of such exposure, where such exposure occurred, and what they did. Analyses of all the variables showed that the frequency of respiratory illnesses among Hong Kong mothers was highly related to their reports of previous exposure to dust or gas fumes (table 7) in the workplace.

Overall, some 21.7% (n = 68) of the total sample of Hong Kong mothers reported a previous history of occupational exposure to dust, and 11.5% (n = 36) to gas/fumes. The percentages of exposed mothers with one or more respiratory illnesses increased proportionately with the degree of reported severity of exposure to such air pollutants in a dose-response manner. Among those exposed to severe levels of either pollutant, the attributable risk was calculated to be

55%. Gas fumes seemed to exert a larger effect than did dust, as the attributable risk was 45.6% for the former versus 33.8% for the latter.

Although the same questions were not asked in the Japanese survey, data on Japanese mothers currently employed in dusty industries such as mining showed no relationship with their prevalence of respiratory illnesses. In addition, when comparing the lifestyle profiles of the 2 populations (table 8), it can be seen that mothers in Japan were less likely to work outside the home, so that their likelihood of being exposed to such occupational exposures would be less than that of the Hong Kong mothers.

In terms of possible sources of indoor air pollutants in the home, the data did not help explain the discrepancy in prevalence rates in the 2 populations. Some 60% of the Japanese fathers were current smokers versus only 36% of the Hong Kong fathers. Although cooking styles are greatly different between the 2 populations, with Chinese cooking methods more likely to produce cooking fumes because of the stir-fry method, the percentages of kitchens with mechanical ventilation fans/hoods was the same in both populations, i.e., 79 to 80%.

It was interesting to note that the mean household size was statistically different (p = 0.000), with Hong Kong families averaging 5.31 persons versus 4.54 persons in Japan. The effects of family size on the frequency of respiratory illnesses are shown in table 9. There was a tendency for Hong Kong mothers living in larger households to report more respiratory illness than those living in smaller ones. However, such was not the case for the Japanese mothers. Moreover, among the Hong Kong mothers, no relationship was found between household density, i.e., the total number of people in the family

TABLE 9  
RELATIONSHIP OF FAMILY SIZE TO RESPIRATORY ILLNESSES  
AMONG HONG KONG AND JAPANESE MOTHERS\*

Household Size	Total Number of Mothers	Mothers with $\geq 1$ Respiratory Illnesses†		
		(n)	(%)	Relative Risk
Hong Kong				
Small, $\leq 4$	100	22	22.0	1.00
Medium, 5 to 6	155	37	23.9	1.09
Large, 7+	59	19	32.2	1.46
Total	314	78	24.8	
Japan				
Small, $\leq 3$	28	5	17.9	1.00
Medium, 4 to 5	175	40	22.9	1.28
Large, 6+	40	9	22.5	1.26
Total	243	54	22.2	

\* Pearson's correlation coefficient significance and p values: Presence and absence of illnesses in Hong Kong:  $r = 0.024$ , p = 0.33; in Japan:  $r = 0.025$ , p = 0.35. Exact number of illnesses in Hong Kong:  $r = 0.078$ , p = 0.09; in Japan:  $r = 0.034$ , p = 0.30.

† The presence of the following respiratory illnesses unrelated to cold/flu: cough  $\geq 3$  months, phlegm  $\geq 3$  months, pneumonia, allergic rhinitis, bronchitis, asthma, TB, and other chest diseases.

TABLE 10  
RELATIONSHIP OF HOUSEHOLD DENSITY WITH RESPIRATORY  
ILLNESSES AMONG HONG KONG MOTHERS\*

People per Room (n)	Total Number of Mothers	Mothers with $\geq 1$ Respiratory Illnesses†		
		(n)	(%)	Relative Risk
Low, $\leq 2.49$	81	20	24.7	1.00
Medium, 2.5 to 3.5	105	23	21.9	0.89
High, $> 3.5$	128	35	27.4	1.11
Total	314	78	24.8	

\* Pearson's correlation coefficient and  $p$  values: presence and absence of diseases  $r = 0.031$ ;  $p = 0.29$ ; exact number of diseases  $r = 0.008$ ;  $p = 0.44$ .

† The presence of the following respiratory diseases unrelated to cold/flu: cough  $\geq 3$  months; phlegm  $\geq 3$  months; pneumonia; allergic rhinitis; bronchitis; asthma; TB; and other chest diseases.

divided by the number of rooms they occupied, and the frequency of respiratory illnesses (table 10). The Japanese data did not contain information on household density for comparative analysis.

#### Discussion

The findings of this preliminary epidemiologic study on the prevalence of respiratory illnesses among never-smoked mothers and children in Hong Kong and Tokyo suggest that such illnesses are much more common in Hong Kong. Hong Kong subjects were 10 or more times more likely than their Japanese counterparts to report symptoms of chronic cough and phlegm expectoration exceeding 3 months duration.

The differences in reported frequencies of respiratory illnesses were greatest in the comparison of school children. Hong Kong children were 4.5 times more likely to have had a previous history of wheezing, and 8 times more likely to have had pneumonia than were Japanese children. Overall, 25.2% of the Hong Kong children versus 18.7% of the Japanese children had one or more of the surveyed chest illnesses, and their mean numbers of chest illnesses per sick child were 1.96 and 1.31, respectively. All of these differences were statistically significant, with the comparison of those with chest illnesses borderline significance ( $p = 0.066$ ).

We feel that the interpretation of these findings must be viewed in light of the degree of medical knowledge of the 2 populations. For a mother to report that she or her child had suffered from such diseases as bronchitis, pneumonia, asthma, tuberculosis, or allergic rhinitis, she would have had to have been told by a doctor of such a diagnosis/description of the problem. Because doctor-patient communication is poor in Hong Kong, and patients are frequently not told the diagnosis nor the names of the drugs that are prescribed, the knowledge/usage of

such medical terms among the population would be infrequent. This would be especially true among the working-class mothers whose average educational attainment is primary school only (11). Thus, these illnesses, which we have labeled as "respiratory diseases," would tend to be underreported in the Hong Kong population. On the other hand, such common descriptive terms as cough, phlegm expectoration, and wheezing are well understood by all, and thus the survey was able to reflect a more accurate recording of the prevalence of these symptoms.

Evidence for the fact that the greater unfamiliarity with medical terms among the Hong Kong mothers seemed to influence their reported frequencies is reflected in the unrealistically low reporting rate of tuberculosis. Only 1.6% of the Hong Kong versus 2.1% of the Japanese mothers reported having such a history. Yet it is known that the real rate should be much higher in Hong Kong since tuberculosis is still a common infectious disease in that community, with 137.4 new cases/100,000 population reported and a mortality rate of 8.4/100,000 (12) registered in 1983. The comparable incidence and mortality rates for Japan in 1985 were 48.4/100,000 and 3.9/100,000.

The Hong Kong subjects also reported more respiratory illnesses per person than did the Japanese subjects. These differences were especially notable among the children where the group mean values showed the Hong Kong children to be more than 2.9 times higher than those of the Japanese children ( $t$  test,  $p$  value = 0.001). No differences were observed in the frequencies of these illnesses by sex of the child.

Although the Hong Kong children were on average 8.5 months older than the Japanese children, we did not feel that this slight age difference could account for the large differences observed in the

Hong Kong children's higher reported frequencies of respiratory illnesses. In addition, the children in both populations have been immunized with the generally recommended schedule of diphtheria, pertussis, polio, BCG, etc. vaccines, so these differences were not due to immunization rates.

For both populations, however, there was a highly significant correlation between the frequency of respiratory illnesses of each mother and her child. Mothers who reported one or more illnesses for themselves were about twice as likely to report a similar number for their children.

For the Hong Kong mothers, a significant relationship was detected with increasing exposure to dust/smoke or gas/fumes in the workplace. The occurrence of respiratory illnesses seemed to be related to occupational exposures to such pollutants in 34% of those ever exposed to dust/smoke, and 46% of those ever exposed to gas/fumes. For the Hong Kong population as a whole, the attributable risk percentage was 10.0% for the former and 8.8% for the latter. However, analysis of the data by whether the mother was currently employed or not did not show any significant differences in the reported frequencies of respiratory illnesses for herself or her child.

The consistent tendency for Hong Kong subjects to have higher prevalence rates of respiratory illnesses than their Japanese counterparts is difficult to explain. Although, as shown above, some relationship was found with previous occupational exposure to dust or fumes in the workplace, the percentages of mothers currently working was not statistically different in the 2 groups.

The role of indoor air pollution in the home from passive smoking or heating/cooking activities has been investigated. Japanese fathers were about twice as likely to be smokers than were Hong Kong fathers. Moreover, in another report on the Hong Kong mothers (13), no association was found between the prevalence of chronic cough or sputum and the smoking patterns of their husbands. The etiologic role of cooking activities is also doubtful, as the proportion of kitchens with mechanical ventilation such as fans or cooking hoods was not different in Tokyo and Hong Kong. Previous case-control studies on the role of cooking fuels in lung cancer risk among females in Hong Kong (14) and Japan (15) did not find an association between fuel type (i.e., kerosene, liquid petroleum gas, charcoal, and wood/grass) and lung cancer risk.

2023379766

Among the variables compared, Hong Kong families tended to be significantly larger, averaging 5.31 persons versus 4.54 for Japanese households. Among Hong Kong mothers, some association was found between larger household size and the frequency of respiratory illnesses, but such was not the case for household density. Moreover, larger household size was not associated with more respiratory illnesses among the Japanese mothers. Although both household size and density are related with socioeconomic status, the lack of an association with household density in Hong Kong would seem to indicate that these variables were not simply surrogate measures of household income. This is because, with the extremely expensive rental situation in Hong Kong, higher density living is directly associated with less income, whereas household size may reflect the persistence of an extended family system and, traditionally, according to the Confucian ethos, 3-generation families are desirable.

Several possibilities may help explain the patterns of respiratory illnesses in both populations. Recall bias may play a role as there was an increasing tendency for mothers reporting one or more respiratory illnesses for themselves to report the same for their children. This tendency was found in both the Japanese and the Hong Kong mothers, so it would not explain their highly different prevalence rates of respiratory illnesses. The principle of recall bias may have operated also on the finding that occupational exposures were related to respiratory illnesses among the Hong Kong mothers, since those with such illnesses may have been more likely to recall such past exposures than those without such problems. However, occupational exposures to such pollutants could only account for 9 to 10% of the respiratory illnesses in the Hong Kong mothers.

The role of cross infection, i.e., mother to child or other household members to mother or child, seems suggested by: (1) the direct association between household size and frequency of respiratory illnesses in the Hong Kong mothers, (2) the correlation between multiple respiratory illnesses within each mother-child pair in both populations, and (3) that Hong Kong families were significantly larger than Japanese families. However, no such association was found with household density, which would seem a more direct measurement of the potential for cross infection since the chances of spreading infectious respiratory diseases should be correlated with higher household densities. It appears that other not yet identi-

fied environmental factors are needed to explain these results.

The findings of this study, showing mothers and especially children in Hong Kong to have larger numbers of sick subjects and to have more illnesses per subject than their Japanese counterparts, are consistent with the findings of other surveys in both areas. Questions added to an international survey in 1986 on passive smoking and urinary cotinine levels sponsored by the International Agency for Research on Cancer indicated that women in Hong Kong were about 10 times more likely to report symptoms of chronic cough or phlegm than were women in Sendai, Japan. A population survey of respiratory illnesses in Japan in 1983 (T. Mori, personal communication) indicated that the reported age-adjusted rates of such illness for non-smoking women in Japan were similar to those reported among the Japanese mothers in this survey. Thus, we feel that the reported differences in the frequencies of respiratory illnesses in Hong Kong and Japan are not artifactual.

These results agree with the contrasting female lung cancer incidence rates in the 2 areas. The epidemiologic data showed that chronic bronchitis was associated with increased risk for lung cancer in females (1). Moreover, the multistage model of carcinogenesis makes this association biologically plausible since these symptoms result from and result in a chronic irritation effect on the respiratory tract, making it more susceptible to the action of carcinogenic initiators or promoters. Previous occupational exposure to dust or fumes was associated with respiratory illnesses in the Hong Kong mother, and frequencies of such illnesses in the mother were directly related to those in her child. Although this could account for a portion of the respiratory illnesses, more investigation is needed to find other etiologic agents in the Hong Kong environment to account for the higher frequency of respiratory health problems. A recent time-trend analysis by Barker and Osmond (16) in England and Wales showing that respiratory diseases in childhood led to higher mortality rates from chronic bronchitis and emphysema later in adult life, ominously suggests that the high rates of childhood respiratory illnesses found in the Hong Kong population today portends to excess mortality from respiratory diseases in the future when these children reach 40+ yr of age.

#### Acknowledgment

The writers thank the Director of Education

of Hong Kong for his advice and permission to carry out this study; the headmaster and teachers of the S. K. H. Kei Hin Primary School in Hong Kong for their kind assistance in the field work; Mr. H. C. Kwan of the Radiotherapy Department of the Queen Elizabeth Hospital for data collection; the Air Policy Group of the Environmental Protection Department of the Hong Kong government for data on air pollution; Dr. P. Witorsch for his comments on chest symptoms; Ms. C. Y. Ho for data management; Mr. K. Li for statistical work; and Mrs. T. Lam, Ms. A. Chow, and Ms. M. Chi for secretarial assistance.

#### References

1. Koo LC, Ho JH-C, Lee N. An analysis of some risk factors for lung cancer in Hong Kong. *Int J Cancer* 1985; 35:149-55.
2. Doll R, Hill AB. A study on the aetiology of carcinoma of the lung. *Br Med J* 1952; 2:1271-86.
3. Wynder EL, Bross IJ, Cornfield J, O'Donnell WE. Lung cancer in women. *N Engl J Med* 1956; 255:1111-21.
4. Samet JM, Humble CG, Pathak DR. Personal and family history of respiratory disease and lung cancer risk. *Am Rev Respir Dis* 1986; 134:466-70.
5. Wu AH, Henderson BE, Pike MC, Yu MC. Smoking and other risk factors for lung cancer in women. *J Natl Cancer Inst* 1985; 74:747-51.
6. Hong Kong Cancer Registry. Cancer incidence in Hong Kong, 1982. Hong Kong: Hong Kong Government's Medical and Health Department Institute of Radiology and Oncology, Queen Elizabeth Hospital, 1982.
7. Hanai A, Kitamura H, Fukuma S, Fujimoto I, eds. Cancer incidence in Japan 1975-1979. Osaka: Osaka Cancer Registry, 1984; 17.
8. Ferris BG. Epidemiology standardization project. *Am Rev Respir Dis* 1978; 118:1-120.
9. Medical Research Council Committee on the Aetiology of Chronic Bronchitis. Standardized questionnaires on respiratory symptoms. *Br Med J* 1960; 2:16658.
10. Osborn JF. Basic statistical methods for epidemiological studies. London: London School of Hygiene and Tropical Medicine, Division of Medical Statistics and Epidemiology, 1986; 16-17, 70.
11. Census and Statistics Department. Hong Kong Government. Hong Kong 1981 census: basic tables. Hong Kong: Government Printer, 1982 (no. 496778-59L-3/82, p. 12).
12. Director of Medical and Health Services. Hong Kong Annual Departmental Report, 1983-1984. Hong Kong: Government Printer, 1984 (no. 119716-23L-11/84).
13. Koo LC, Ho JHC. Environmental tobacco smoke: lifetime evaluations of dose and lung cancer risk among never-smoked Chinese females in Hong Kong. International Conference on Indoor Air Quality Abstracts. Tokyo: The Council for Environment and Health, Nov. 4-6, 1987; 36.
14. Koo LC, Lee N, Ho JHC. Do cooking fuels pose a risk for lung cancer?: a case-control study of women in Hong Kong. *Ecology Dis* 1983; 2:255-65.
15. Shimizu H. A case-control study of lung cancer by histologic type. *J Jpn Lung Cancer Assoc* 1983; 23:127-37.
16. Barker DJP, Osmond C. Childhood respiratory infection and adult chronic bronchitis in England and Wales. *Br Med J* 1986; 293:1271-5.

2023379767

2023379768



Melia, R.J.W., Chinn, S., Rona, R.J. "Respiratory illness and home environment of ethnic groups" British Medical Journal 296:1438-1441, 1988.

**ABSTRACT:** Factors contributing to differences in the prevalences of respiratory symptoms and diseases among ethnic groups were studied in primary schoolchildren living in 20 innercity areas of England in 1983. The raised prevalences of respiratory symptoms in these groups were compared with results from a national representative sample of children studied in 1982. Data on age, sex, respiratory illness, and social and environmental variables were obtained by questionnaire for 4815 children living in innercities. The children were classified as white, Afro-Caribbean, Urdu, Gujarati, Punjabi, other Asian, or "other." Significant differences in the prevalence of respiratory conditions were found among the ethnic groups after allowance was made for the effects of interfering variables. Except for asthma all conditions were most prevalent in Afro-Caribbeans and whites. In these two ethnic groups respiratory illness was significantly associated with belonging to a one parent family and the combined use of gas cookers and paraffin heaters at home.

Respiratory illness was found to vary in prevalence among ethnic groups but may be perceived differently by different groups. Further studies, measuring lung function, are necessary.

2023379769

Thus any benefit of anticoagulants is likely to be modest, and a large randomised trial would be required to detect it reliably. Of course, any modest benefit would be offset by the complexity, side effects, and cost of the treatment; in any case, a rather small population of patients with stroke are eligible for such treatment.<sup>12</sup> On the other hand, our negative results, based on a non-randomised comparison and with fairly wide confidence intervals, are unlikely to convince doctors who are already using long term anticoagulant treatment despite the lack of good data to support their opinion. To resolve this dilemma we are planning a three year randomised trial of 1200 patients to compare treatment with anticoagulants, aspirin, and placebo.

The Oxfordshire community stroke project is funded by the British Medical Research Council and the Chest, Heart, and Stroke Association. The Dutch Heart Foundation supported J.L. during a visit to Oxford for three months.

## References

1. Furian AS, Cassner SJ, Mohr RL, et al. Hemorrhage and anticoagulation after non-atrial embolic brain infarction. *Neurology* 1982;32:296-2.
2. Cerebral Embolism Study Group. Immediate anticoagulation of embolic stroke: a randomised trial. *Stroke* 1983;14:664-76.
3. Lødder J, van der Lugt P, JM. Evaluation of the risk of immediate anticoagulation treatment in patients with embolic stroke of cardiac origin. *Stroke* 1983;14:42-6.
4. Keller RL, Berger JR, Alter M, et al. Cerebral ischemia and atrial fibrillation: prospective study. *Neurology* 1984;34:1285-91.
5. Martin GJ, Baker J. Non-atrial cerebral emboli of cardiac origin. *Arch Intern Med* 1984;144:1997-9.
6. Sæviak I, Wærnes CP. The secondary prevention of stroke in patients with atrial fibrillation. *Arch Neurol* 1986;43:66-8.
7. Sherman DG, Hart RG, Easton JD. The secondary prevention of stroke in patients with atrial fibrillation. *Arch Neurol* 1986;43:68-70.
8. Machuga V. Atrial fibrillation and recurrent stroke. *Arch Neurol* 1986;43:70.
9. Keller RL. Recurrent embolic cerebral infarction and anticoagulation. *Neurology* 1982;32:283-5.
10. Norving B, Nilsson B. Cerebral embolism of cardiac origin: the limited possibilities of secondary prevention. *Acta Neurol Scand* 1986;73:520.
11. Gustafsson C, Britton M. Prognosis after brain infarction in patients with non-valvular atrial fibrillation compared with sinus rhythm. *Acta Neurol Scand* 1986;73:520-1.
12. Sandercock P, Bamford J, Warlow C, Peeto R, Sæviak I. Is a controlled trial of long-term oral anticoagulants in patients with stroke and non-rheumatic atrial fibrillation worthwhile? *Lancet* 1986;1:785-92.
13. Lødder J. A prospective study on the risk of immediate anticoagulation in cardiac embolic stroke. In: Siebert T, Schumacher K, Gensert D, Sæviak I, eds. *Cerebral arterial system control of the brain*. Boston: Martinus Nijhoff, 1986:245-8.
14. Oxfordshire Community Stroke Project. Incidence of stroke in Oxfordshire: first year's experience of a community stroke register. *Br Med J* 1983;287:715-7.
15. Peeto R, Pike MC, Armitage P, et al. Design and analysis of randomised clinical trials requiring prolonged observation of each patient. II. Analysis and examples. *Br J Cancer* 1977;35:1-39.
16. Pessin MS, Huston RC, Davis KR. Mechanisms of acute cerebral stroke. *Arch Neurol* 1979;36:245-52.
17. Yusuf S, Peeto R, Lewis J, Collins R, Sleight P. Beta blockade during and after myocardial infarction: an overview of the randomised trials. *Prog Cardiovasc Dis* 1985;27:335-71.
18. Sage JH, Van Cleet RL. Risk of recurrent stroke in patients with atrial fibrillation and non-valvular heart disease. *Stroke* 1983;14:537-40.

(Accepted 16 December 1987.)

# Respiratory illness and home environment of ethnic groups

R J W MELIA, S CHINN, R J RONA

## Abstract

Factors contributing to differences in the prevalences of respiratory symptoms and diseases among ethnic groups were studied in primary schoolchildren living in 20 inner city areas of England in 1983. The raised prevalences of respiratory symptoms in these groups were compared with results from a national representative sample of children studied in 1982. Data on age, sex, respiratory illness, and social and environmental variables were obtained by questionnaire for 4815 children living in inner cities. The children were classified as white, Afro-Caribbean, Urdu, Gujarati, Punjabi, other Asian, or "other." Significant differences in the prevalence of respiratory conditions were found among the ethnic groups after allowance was made for the effects of interfering variables. Except for asthma all conditions were most prevalent in Afro-Caribbeans and whites. In these two ethnic groups respiratory illness was significantly associated with belonging to a one parent family and the combined use of gas cookers and paraffin heaters at home.

Respiratory illness was found to vary in prevalence among ethnic groups but may be perceived differently by different groups. Further studies, measuring lung function, are necessary.

## Introduction

The health of ethnic minority groups in the United Kingdom has been the subject of considerable discussion and concern during the past two decades. Inherited disorders such as sickle cell anaemia and illnesses such as rickets have been highlighted.<sup>1,2</sup> Respiratory health has not been studied thoroughly, though a higher prevalence of respiratory illness has been reported in West Indians<sup>3</sup> and respiratory illness in infants was reported to be more common among Bengalis than the indigenous population of an inner city area.<sup>4</sup> The cause of these differences has not been studied in detail, although poor social circumstances are probably a factor in some ethnic groups. As respiratory disease in childhood has been linked with susceptibility to respiratory disease in later life<sup>5</sup> it is important to investigate the causes of variation in respiratory health between children of different ethnic groups to identify preventive measures.

This study of primary schoolchildren investigated the prevalence of respiratory illness in ethnic groups in inner city areas and factors that contribute to differences in prevalence among the ethnic groups and between the groups from inner cities and a national sample of children.

## Subjects and methods

In 1983 data on respiratory symptoms and diseases were collected in the national study of health and growth, a surveillance study of primary schoolchildren that included white, Afro-Caribbean, Indian, and Pakistani children from inner city areas, most of whom had spent most of their lives in Britain. Twenty wards in England with a high percentage of children of Afro-Caribbean and Indo-Pakistani ethnic origin and children living in inner city areas with a high level of overcrowding, unemployment, or lack of exclusive use of amenities had been selected, and about 350 children aged 5-11 from one or two schools close to the geographical centre of each ward had been studied. In 1983 the study investigated ethnic minorities for the first time. Several factors were studied in connection with respiratory disease but smoking was not one of them. To assess further the size of the

Department of Community Medicine, United Medical and Dental Schools of Guy's and St Thomas's Hospitals, London SE1 7EH

R J W MELIA, PHD, lecturer in epidemiology

S CHINN, MA, senior lecturer in medical statistics

R J RONA, PHD, MFCM, senior lecturer in community medicine

Correspondence to: Dr Melia

problem of respiratory disease in inner cities were included in our study data on white primary schoolchildren from the 1982 national study of health and growth; these children had a similar social class distribution to other representative national samples.<sup>11</sup> The methods of collecting data closely resembled those used in 1983, although data on 'colds going to the chest' were not collected.

In 1983 data on respiratory illness in the children were collected from a questionnaire completed by a parent of each child. The questionnaire was available in English, English and Urdu, English and Gujarati, and English and Punjabi. It asked whether the child usually had a cough first thing in the morning, cough during the day or night, or colds that 'went to the chest'; whether the child's chest ever sounded wheezy or whistling, and how many attacks of bronchitis or asthma had been experienced during the past 12 months. Other questions were asked about the number of children at home, father's occupation, mother's educational attainment, uptake of free school meals, and types of fuel used for cooking and heating at home. Ethnic group was ascertained from statements made by fieldworkers and the main language spoken at home.

Prevalences of respiratory conditions were compared with the  $\chi^2$  test and by logistic regression using the computer program GLIM.<sup>12</sup> As the respiratory conditions were interrelated an overall measure of respiratory illness (the presence of one or more respiratory conditions) was also used. Two main groups of regression analyses were carried out on the 1983 sample. Firstly, ethnic groups were compared allowing for age, sex, area of residence, mother's educational attainment, and number of children at home. Areas of residence was included as the ethnic minority groups came mainly from the areas specifically selected to include those groups, and the prevalence of respiratory illness in children might be related to environmental factors not otherwise considered in our analyses. Mother's educational attainment, classified into three groups (no formal education or primary only, primary and secondary, college or university), was used instead of social class to indicate social circumstances. Secondly, for whites and Afro-Caribbeans the additional effects of living in a one parent family and living in a home with a gas cooker or paraffin heaters were studied. Gas cookers and paraffin heaters are indoor sources of air pollution, particularly nitrogen dioxide.<sup>13</sup> Homes were placed in one of three groups according to the expected level of nitrogen dioxide: homes with an electric cooker and no paraffin heaters, homes with a gas cooker and no paraffin heaters, and homes with both a gas cooker and paraffin heaters. Homes with paraffin heaters alone or with coal fires, another important source of indoor air pollution, were excluded because their numbers were too small (living in a one parent family and the effects of indoor air pollution could not be studied in the Asian groups because the question on one parent families had been incorrectly translated and too few homes had electric cookers or paraffin heaters less than 15 and less than seven, respectively in each Asian group).

Additional regression analyses were carried out to compare respiratory symptoms between white children studied in 1982 and 1983. The effects of age, sex, father's social class, living in a one parent family, mother's education, and number of children at home were allowed for in this comparison.

## Results

Data on 4815 children (67.8% of the 7103 children in the 1983 sample) were obtained. Absence of data on age, sex, or ethnic group excluded 382 children, and absence of data on the air respiratory conditions, mother's education, or type of fuel used for cooking excluded a further 1906. The response rate varied among ethnic groups, with Afro-Caribbeans having a response rate of 58%, Urdu 69%, 'other ethnic groups' 56%, and each remaining group more than 70%. The 2105 white children from the 1983 sample were compared with 4849 white children from the 1982 sample (70.7% of the 6862 studied). These samples were similar in their age and sex distributions.

Tables I and II show the unadjusted prevalences of respiratory symptoms and diseases in boys and girls studied in 1983 by ethnic group. The prevalence of all conditions except cough in the morning in both sexes and asthma in boys varied significantly among ethnic groups ( $p < 0.01$ ). In both sexes cough during the day or night and colds going to the chest tended to be most prevalent in whites and Afro-Caribbeans. Bronchitis was most prevalent in whites, and wheezing in whites and Afro-Caribbeans. For the other respiratory conditions, differences in prevalence among ethnic groups were inconsistent between the sexes. The overall measure of respiratory illness, the presence of one or more respiratory conditions, was found most commonly in Afro-Caribbeans and least commonly in Gujaratis. The prevalences in whites were high but only compared with those in the other ethnic groups but also compared with those in the 1982 sample.

Each respiratory condition was analysed separately for the effects of age, sex, mother's education, number of children in family, and area of residence. The prevalence of all conditions except asthma declined significantly with age ( $p < 0.05$ ) and tended to be higher in boys than girls. The prevalences showed some association with mother's education, tending to be highest among children of mothers with no formal education or only elementary education and lowest among children whose mothers had been to college or university, but significantly so only for coughs ( $p < 0.05$ ). The presence of four or more children in the family was associated with high prevalences of coughs ( $p < 0.05$ ), but the other conditions were reported most commonly for single children ( $p < 0.05$ ). Area of residence was related to the prevalence of cough in the morning, wheezing, and bronchitis ( $p < 0.05$ ). The first order interactions among these independent variables

TABLE I.—Unadjusted percentage (number) of respiratory conditions by ethnic group among boys

	White						Total	
	1982 (n=2487)	1983 (n=1089)	Afro-Caribbean (n=261)	Urdu (n=157)	Gujarati (n=221)	Punjabi (n=451)	Other Asian (n=110)	Other (n=140)
Cough in the morning	3.5 (68)	7.7 (84)*	8.8 (33)	9.9 (15)	9.6 (8)	8.4 (38)	4.5 (5)	9.6 (5)
Cough during day or night	7.3 (135)	19.6 (170)*	18.4 (68)	8.9 (14)	8.1 (11)	10.9 (45)	8.2 (9)	9.3 (13)
Wheezing	11.1 (206)	15.9 (146)*	16.9 (60)	10.2 (16)	5.9 (13)	10.9 (48)	7.3 (8)	10.6 (14)
'Colds going to chest'	34.2 (672)	34.7 (322)	33.3 (127)	19.7 (31)	17.2 (38)	21.5 (97)	25.5 (28)	26.4 (37)
Bronchitis	3.7 (73)	7.5 (68)*	3.4 (9)	1.3 (2)	1.8 (4)	3.8 (17)	5.5 (6)	2.1 (3)
Asthma	3.0 (57)	5.9 (53)	1.5 (4)	6.4 (10)	2.3 (5)	4.7 (21)	3.6 (4)	5.7 (8)
One or more respiratory conditions	40.9 (845)	41.8 (381)	41.8 (156)	28.0 (44)	23.1 (51)	28.4 (128)	30.0 (33)	33.4 (47)

\*Tukey, 1982 v 1983,  $\chi^2$  test,  $df=1$ ,  $p < 0.001$

†All ethnic groups, 1983 v 1982,  $\chi^2$  test,  $df=6$ ,  $p < 0.001$

TABLE II.—Unadjusted percentage (number) of respiratory conditions by ethnic group among girls

	White						Total	
	1982 (n=2332)	1983 (n=1016)	Afro-Caribbean (n=284)	Urdu (n=166)	Gujarati (n=220)	Punjabi (n=436)	Other Asian (n=108)	Other (n=136)
Cough in morning	3.8 (90)	7.3 (74)**	9.9 (28)	4.8 (18)	7.3 (16)	5.5 (24)	10.2 (11)	7.1 (16)
Cough during day or night	6.2 (145)	15.2 (154)**	16.5 (47)	9.6 (36)	10.5 (23)	8.5 (37)	13.0 (14)	12.5 (20)
Wheezing	8.1 (190)	11.6 (118)*	12.0 (34)	12.0 (46)	5.5 (12)	6.7 (29)	5.6 (6)	6.6 (10)
'Colds going to chest'	32.7 (832)	32.7 (332)	30.6 (87)	15.1 (55)	12.7 (28)	14.7 (64)	21.3 (23)	24.7 (40)
Bronchitis	2.2 (51)	5.4 (55)**	4.2 (12)	3.8 (14)	0.9 (2)	3.0 (13)	0.0 (0)	3.7 (5)
Asthma	1.9 (44)	1.1 (11)	2.1 (6)	3.6 (16)	0.5 (1)	2.5 (11)	4.6 (5)	3.8 (5)
One or more respiratory conditions	34.7 (838)	39.1 (411)	39.1 (111)	24.7 (91)	19.1 (42)	23.2 (101)	26.9 (29)	31.7 (52)

\*Tukey, 1982 v 1983,  $\chi^2$  test,  $df=1$ ,  $p < 0.01$ , \*\* $p < 0.001$

†All ethnic groups, 1983 v 1982,  $\chi^2$  test,  $df=6$ ,  $p < 0.001$

each respiratory symptom were not significant. Significant differences in the prevalence of all conditions were found among the ethnic groups ( $p < 0.05$ ), after allowance was made for the effects of the independent variables. These results were similar to those for the unadjusted prevalences and are illustrated in table III adjusted to boys aged 8 with a mother with secondary school education and with one sibling.

The second set of regression analyses, conducted in 2022 whites and 530 Afro-Caribbeans, studied additionally the effects of belonging to a one parent family and of living in a home in which gas cookers or paraffin heaters were used. Table IV gives the relative risk of respiratory conditions associated with mother's education, number of children in the family, belonging to a one parent family, and use of gas cookers and paraffin heaters. Results for asthma and bronchitis showed no significant relation to any of these factors and are not shown. High risks of all the conditions shown in table IV were associated with one parent families compared with two parent families ( $p < 0.05$ ). The risk of respiratory illness increased when two or more sources of nitrogen dioxide (a gas cooker and paraffin heaters) were present in the home. The association between gas cookers alone and respiratory illness approached significance for cough in the morning and wheeze ( $p < 0.1$ ). The association between respiratory illness and the combined use of a gas cooker and paraffin heaters was significant for colds going to the chest and the presence of one or more respiratory conditions ( $p < 0.05$ ). For a subset of 2164 whites and Afro-Caribbeans regression analysis of each respiratory condition was conducted to include father's social class and uptake of free school meals. The effects on respiratory illness of one parent families and the combined use of gas cookers and paraffin heaters remained significant for colds going to the chest ( $p < 0.05$ ) and borderline for the overall measure ( $p = 0.052$ ).

To assess further the problem of respiratory illness in inner cities the prevalence of respiratory conditions in the 1983 sample of white children was compared with the prevalence in the 1982 national representative sample after allowance had been made for the effects of interfering variables. The prevalences of cough in the morning, cough during the day or night, wheezing, and bronchitis were significantly higher in 1983 than 1982 ( $p < 0.05$ ).

## Discussion

In our study Afro-Caribbeans and white people living in inner cities had higher prevalences of several conditions compared with Asians. In a national cohort of children the prevalence of wheezing was significantly higher in children with West Indian and British parents than those with Asian parents ( $p < 0.01$ ), but the prevalence

of asthma and bronchitis did not differ among ethnic groups. West Indian and Bengali infants have been reported to attend accident and emergency departments because of respiratory disease more commonly than white children, but this may partly reflect a different pattern of use of health services by ethnic groups. Smith found asthma and wheezing in 5-6 year olds to be more prevalent in West Indians born in England than in Asians born in England or abroad. It is unclear, however, which groups of Asians were being studied. In our study the prevalence of asthma differed among groups of Asians.

The differing results of studies may be explained partly by differences in methodology and partly by biases in the results. Three main biases should be considered. Firstly, certain ethnic groups such as Punjabis are not homogeneous, and subgroups would be expected to differ in health. The distribution of these subgroups varies in England, and a study in one area is likely to contain only one subgroup. Each ethnic group in our study lived in several areas of England, so our results cover a range of children within each group. Secondly, respiratory illness may well be perceived differently by each ethnic group, and these differences may not have been dealt with simply by translating the questionnaire. Although studies of the incidence and prevalence of respiratory disease indicate the burden of respiratory disease experienced by some groups, objective measures of respiratory ill health, such as lung function, would contribute further to the study of respiratory illness in ethnic groups. Thirdly, in this study response rates varied among ethnic groups even though non-responders were followed up by health visitors and the questionnaire was available in three languages. Inclusion of non-responders known to have respiratory illness, however, made no difference to our results. The relation of respiratory illness to factors such as age was similar to previous findings, which gives some credence to our results.

A raised prevalence of respiratory illness might be expected in large families<sup>10</sup> and when the mother's educational level is low, this being associated with poor social class,<sup>11</sup> but such was not the case in this study. Single children had significantly more colds going to the chest and more wheezing ( $p < 0.05$ ) than children with three or more siblings. A mother with only one child to care for may be more aware of that child developing respiratory illness than mothers with larger

TABLE III—Mean prevalence (expressed as percentage and number) of respiratory conditions adjusted to boys aged 8 with mother educated up to secondary school and two children in family. Figures in each group are for the 1983 sample

	White (n = 2105)	Afro-Caribbean (n = 545)	Urdu (n = 323)	Gujarati (n = 441)	Punjabi (n = 887)	Other Asian (n = 218)	Other (n = 296)	Total (n = 4815)
Cough in morning	4.4 (158)	5.9 (51)	3.2 (23)	2.7 (24)	2.6 (62)	3.7 (16)	2.5 (13)	5.5 (347)*
Cough during day or night	14.4 (324)	15.8 (95)	6.9 (30)	7.3 (41)	6.3 (82)	8.3 (23)	10.4 (616)**	
Wheezing	11.7 (267)	10.8 (73)	8.7 (36)	5.3 (25)	5.7 (78)	4.8 (14)	7.3 (24)	8.8 (537)**
"Colds going to chest"	36.7 (704)	34.4 (174)	20.8 (56)	17.1 (66)	18.7 (161)	24.9 (51)	28.3 (72)	24.3 (1284)**
Bronchitis	11.6 (138)	4.6 (21)	1.9 (3)	2.6 (16)	6.7 (30)	5.1 (6)	6.0 (19)	4.4 (213)**
Asthma	3.1 (49)	2.2 (10)	7.0 (16)	1.5 (6)	5.0 (32)	4.9 (9)	6.0 (14)	3.4 (136)**
One or more respiratory conditions	46.1 (833)	46.1 (220)	32.8 (85)	25.7 (93)	28.7 (229)	34.6 (62)	37.5 (92)	35.6 (1614)**

\* $p < 0.05$ , \*\* $p < 0.001$  (chi-squared test, df = 6). After allowing for effects of age, sex, mother's educational attainment, number of children in family, and area of residence.

TABLE IV—Relative risk\* (95% confidence intervals) of respiratory conditions in Afro-Caribbean and white children (1983 data, n = 2552) associated with characteristics of family and home.

	No of children	Cough in morning	Cough during day or night	Wheezing	"Colds going to chest"	One or more respiratory conditions
Mother's education						
No formal education or elementary	196	2.15 (1.4 to 3.28)	1.42 (1.04 to 1.89)	1.33 (0.95 to 1.83)	1.11 (0.92 to 1.31)	1.17 (1.0 to 1.33)
College or university	366	0.81 (0.5 to 1.31)	0.67 (0.47 to 0.93)	1.21 (0.91 to 1.53)	0.88 (0.75 to 1.04)	0.88 (0.75 to 1.00)
No of children in family						
2	902	1.54 (1.06 to 2.23)	1.05 (0.75 to 1.46)	0.74 (0.52 to 1.02)	0.83 (0.68 to 0.99)	0.84 (0.70 to 0.99)
3	699	1.82 (1.10 to 3.23)	1.22 (0.87 to 1.68)	0.89 (0.63 to 1.23)	0.85 (0.69 to 1.02)	0.90 (0.76 to 1.06)
≥4	668	1.75 (0.97 to 3.13)	1.07 (0.75 to 1.49)	0.65 (0.45 to 0.93)	0.70 (0.56 to 0.86)	0.77 (0.63 to 0.92)
One parent family	805	1.48 (1.07 to 2.03)	1.49 (1.22 to 1.8)	1.27 (1.02 to 1.56)	1.10 (1.04 to 1.28)	1.18 (1.06 to 1.28)
Cooking and heating fuels						
Gas cookers, no paraffin heaters	1964	1.48 (0.97 to 2.24)	0.93 (0.73 to 1.19)	1.27 (0.98 to 1.64)	1.10 (0.97 to 1.24)	1.06 (0.94 to 1.17)
Gas cookers, paraffin heaters	83	1.85 (0.79 to 4.25)	1.14 (0.64 to 1.90)	1.64 (0.94 to 2.63)	1.40 (1.06 to 1.71)	1.35 (1.09 to 1.59)

\*Relative to risk in white born aged 8 with mother educated up to secondary school, one child in family, two parent family, and no gas or paraffin fuels used in the home.  
†Difference from relative risk of 1.0  $p < 0.05$ .

families to look after. A low educational level of the mother was associated only with a high prevalence of cough ( $p < 0.05$ ). It may be inappropriate to compare educational background of ethnic groups, particularly those educated abroad, as educational categories may not be directly comparable.

Two other factors previously associated with respiratory illness in children—namely, belonging to a one parent family<sup>11</sup> and exposure to indoor air pollution from gas cookers and paraffin heaters<sup>12,13</sup>—could be studied only in Afro-Caribbeans and whites. Belonging to a one parent family is likely to measure poor social circumstances, but a single parent may be more aware of a child developing respiratory illness. The association of respiratory illness with the combined use of gas cookers and paraffin heaters might reflect poor social circumstances as well as high concentrations of nitrogen dioxide indoors, which may sometimes exceed the European Community's directive for outdoor concentrations of nitrogen dioxide. "Parental smoking habit was not analysed, though smoking has been reported to be more common among Afro-Caribbeans and whites than Asians."

This survey highlights the problem of respiratory disease in children living in inner cities. Such disease was significantly more prevalent in whites compared with all groups in the national sample and varied considerably among ethnic groups. Strong evidence suggests that childhood respiratory illness leads to poor respiratory health in adulthood.<sup>14</sup> We intend to study the variation in respiratory illness among ethnic groups further.

We thank Professor W.W. Holland for his encouragement and the doctors, nurses, teachers, clerks, and fieldworkers in the national study of health and growth for their help. This study was supported by grants from the Department of Health and Social Security and the Scottish Home and Health Department.

## References

1. Oppé TE. The health of the coloured child in Great Britain. *Proceedings of the Royal Society of Medicine* 1964;57:321-3.
2. Black J. The difficulties of living in Britain. *Br Med J* 1982;290:615-7.
3. Hood C. Social and cultural factors in health of children of immigrants. *Arch Dis Child* 1971;46:171-5.
4. Smith JM. The prevalence of asthma and wheezing in children. *Br J Dis Child* 1976;70:73-7.
5. Warren E. Health of infants and use of health services by mothers of different ethnic groups in east London. *Community Med* 1984;6:127-35.
6. Britten N, Davies JMC, Colley JRT. Early respiratory experience and subsequent cough and peak expiratory flow rate in 36 year old men and women. *Br Med J* 1987;294:1317-20.
7. Ross RJ, Chinn S. National study of health and growth: social and biological factors associated with height of children from ethnic groups living in England. *Ann Hum Biol* 1986;13:453-71.
8. Ross RJ, Chinn S, Florey CV. Exposure to cigarette smoking and children's growth. *Int J Epidemiol* 1985;14:402-9.
9. Baker RJ, Nelder JA. *The GLIM system release 3: generalised linear interactive modelling*. Oxford: Numerical Algorithms Group, 1978.
10. Collins JJ, Kasap HS, Holland WW. Environmental factors in child mortality in England and Wales. *Am J Epidemiol* 1971;93:10-22.
11. Goldstein BD, Meila RJW, Chinn S, Florey CV, Clark D, Johns MH. The relation between respiratory illness in primary school children and the use of gas for cooking. II. Factors affecting nitrogen dioxide levels in the home. *Int J Epidemiol* 1979;8:339-45.
12. Butler NR, Golding J. *From birth to five*. Oxford: Pergamon Press, 1986.
13. Lander SR, Cortkull R, Irving LM, Holland WW, Colley JRT. Influence of family factors on the incidence of lower respiratory illness during the first year of life. *British Journal of Preventive and Social Medicine* 1976;30:203-12.
14. Raud J. Social class differences in Britain. 2nd ed. London: Grant MacIntyre, 1981.
15. Jennings AJ, Sheldon MG. Review of the health of children in one-parent families. *J R Coll Gen Pract* 1985;35:478-83.
16. Ashkin DHF, Healy C, Tarrant JB. The measurement of nitrogen dioxide levels associated with domestic paraffin (kerosene) heaters. *Harwell Atomic Energy Research Establishment*, 1980.
17. Meila RJW, Florey CV, Chinn S. The relation between respiratory illness in primary school children and the use of gas for cooking. I—Results from a national survey. *Int J Epidemiol* 1979;8:333-4.
18. Council of the European Communities. Council directive of 7 March 1985 on air quality standards for nitrogen dioxide. *Official Journal of the European Communities: Legislation* 1985;28:L87:1-7. (English ed.)

(Accepted 18 January 1988)

## SHORT REPORTS

### Is surgical closure of the back lesion in open neural tube defects necessary?

Early closure of the lesion is believed to be central to the management of open neural tube defects. Non-closure of the defect, however, does not necessarily increase morbidity to mortality.<sup>1-3</sup> Since 1978 open neural tube defects in patients with a poor prognosis have not been closed at our unit, but the patients have received full medical and nursing care, including antibiotics and shunts for hydrocephalus when necessary. We compared these patients with an earlier group who had received early closure as an urgent treatment.

#### Patients, methods, and results

We reviewed patients with open neural tube defects above L2 or hydrocephalus at birth, or both. Altogether 109 had been born between 1964 and 1971 and 105 born between 1978 and 1985. Treatment policies differed only in that children born between 1964 and 1971 had received early closure of the defect whereas for children born between 1978 and 1985 closure had not been performed or had been deferred until they were at least 3 months old. Data were analysed with the statistical package for the social sciences life tables and the Lee-Desu statistic. Patients who died before they developed a complication were included as "censored" data. Mortality and the incidence of hydrocephalus, insertion of a shunt, ventriculitis, and ventriculitis before insertion of a shunt were compared by relating the difference at any time to the standard error of the difference expressed as a standardised normal z statistic.

No significant difference in the sex ratio, number of children born with hydrocephalus, or number of children with a neurological level above L2 was found between the two groups. The table shows that non-closure resulted in a significantly lower incidence ( $p < 0.001$ ) of hydrocephalus, insertion of a shunt, ventriculitis, and ventriculitis before insertion of a shunt during the first few months of life but did not affect mortality throughout the first year. After the first year there was no significant difference in any of the complications between the groups.

Hydrocephalus correlated with ventriculitis ( $p < 0.001$ ) during the first year, among those whose wound was not closed 37 of the 72 patients with hydrocephalus developed ventriculitis compared with six of the 37 without hydro-

Cumulative survival and proportions SE of babies with open neural tube defects without the complications specified at one, three, six, and 12 months

	Months from birth			
	1	3	6	12
Survival				
Early closure:	0.86:0.03	0.78:0.04	0.65:0.05	0.51:0.05
Non-closure:	0.81:0.04	0.73:0.04	0.64:0.05	0.50:0.05
Without hydrocephalus				
Early closure:	0.40:0.07*	0.12:0.05**	0.08:0.05*	0.08:0.05
Non-closure:	0.83:0.05	0.46:0.07	0.25:0.06	0.10:0.05
Without a shunt				
Early closure:	0.64:0.05*	0.18:0.05**	0.13:0.04**	0.11:0.04
Non-closure:	0.76:0.05	0.51:0.05	0.29:0.05	0.13:0.04
Without ventriculitis				
Early closure:	0.84:0.04*	0.64:0.05*	0.58:0.05	0.48:0.06
Non-closure:	0.94:0.03	0.78:0.04	0.69:0.05	0.48:0.06
Without ventriculitis before insertion of a shunt				
Early closure:	0.72:0.05**	0.49:0.06	0.46:0.06*	0.46:0.06
Non-closure:	0.90:0.06	0.85:0.07	0.75:0.09	0.75:0.09

\*Significance of difference between groups  $p < 0.001$

cephalus, and similar results were found for the babies who received early closure.

#### Comment

We are aware of the caution necessary in analysing historical data. Nevertheless, the finding that mortality did not increase when the neural tube lesion was not closed implies, contrary to previous belief, that early closure as an urgent procedure is not essential for an optimal prognosis. Similarly, the incidence of ventriculitis and, more importantly, of ventriculitis before shunting was reduced during the first three months by non-closure of the defect, suggesting that early closure may not be necessary to reduce the risk of ascending infection.

The incidence of both hydrocephalus and insertion of a shunt was

2023379774

Goren, A.I., Hellmann, S. "Prevalence of Respiratory Symptoms and Diseases in Schoolchildren Living in a Polluted and in a Low Polluted Area in Israel" Environmental Research 45: 28-37, 1988.

SUMMARY: Second and fifth grade schoolchildren living in two communities with different levels of air pollution were studied. The parents of these children filled out ATS-NHLI health questionnaires. The prevalence of reported respiratory symptoms and pulmonary diseases was found to be significantly higher among children growing up in the polluted community (Ashdod) as compared with the low-pollution area (Hadera). Logistic models fitted for the respiratory conditions which differed significantly between both areas of residence also included background variables that could be responsible for these differences. Relative risk values, which we calculated from the logistic models, were in the range of 1.47 for cough without cold to 2.66 for asthma for children from Ashdod, as compared with 1.00 children from Hadera.

2023379775

## Prevalence of Respiratory Symptoms and Diseases in Schoolchildren Living in a Polluted and in a Low Polluted Area in Israel<sup>1</sup>

AYANA I. GOREN AND SARAH HELLMANN

Research Institute for Environmental Health, Ministry of Health and Tel Aviv University  
Sackler School of Medicine, Tel Aviv, Israel 60978

Received March 18, 1987

Second and fifth grade schoolchildren living in two communities with different levels of air pollution were studied. The parents of these children filled out ATS-NHLI health questionnaires. The prevalence of reported respiratory symptoms and pulmonary diseases was found to be significantly higher among children growing up in the polluted community (Ashdod) as compared with the low-pollution area (Hadera). Logistic models fitted for the respiratory conditions which differed significantly between both areas of residence also included background variables that could be responsible for these differences. Relative risk values, which were calculated from the logistic models, were in the range of 1.47 for cough without cold to 2.66 for asthma for children from Ashdod, as compared with 1.00 for children from Hadera. © 1988 Academic Press, Inc.

### INTRODUCTION

It is well known that high air pollution concentrations may influence morbidity and mortality from respiratory conditions. However, the health impact of long-term exposure to low concentrations of air pollutants is not fully known. Many surveys have been carried out during the last decades in an effort to detect possible health effects resulting from long-term exposure to low concentrations of air pollution. In these surveys, which were mainly carried out among adults, it was demonstrated that factors such as smoking and occupational exposure are correlated with the incidence and prevalence of respiratory conditions (Colley and Holland, 1967; Colley *et al.*, 1973; Goldsmith and Friberg, 1977; Holland *et al.*, 1969a; Irvine *et al.*, 1980). Since the effects of air pollution on the respiratory tract are relatively low as compared with those of smoking, controlling for such factors in the analysis is crucial.

Many surveys have recently been conducted among young children who are not occupationally exposed and do not smoke (Biersteker and Leeuwen, 1970; Colley and Brasser, 1980; Colley and Reid, 1970; Ferris, 1978a; Goren and Goldsmith, 1986; Holma *et al.*, 1979; Irvine *et al.*, 1980; Lunn *et al.*, 1967; Melia *et al.*, 1981; Mostardi *et al.*, 1981a; Mostardi *et al.*, 1981b; Toyama, 1964).

However, many variables other than smoking and occupational exposure may affect the respiratory system in the same direction as air pollution and should therefore be taken into account in the analysis. Such variables are socioeconomic

<sup>1</sup> This survey was supported by a grant from the Israel Ministry of Health.



status (Colley and Reid, 1970; Goren and Goldsmith, 1986; Holland *et al.*, 1969a, b; Melia *et al.*, 1981; Peat *et al.*, 1980), crowding index (Holma *et al.*, 1979; Leeder *et al.*, 1976; Lunn *et al.*, 1967; Peat *et al.*, 1980), type of fuel used in household (Hasselblad *et al.*, 1981), smoking habits of adults at home (Bland *et al.*, 1978; Cameron *et al.*, 1969; Colley, 1974; Fergusson *et al.*, 1980; Fergusson *et al.*, 1981; Goren and Goldsmith, 1986; Hasselblad *et al.*, 1981; Lebowitz and Burrows, 1976; Leeder *et al.*, 1976; Schilling *et al.*, 1977; Tager *et al.*, 1979; Vedal *et al.*, 1984; Ware *et al.*, 1984), and respiratory diseases among family members of the observed children (Colley, 1974; Goren and Goldsmith, 1986; Higgins and Keller, 1975; Leeder *et al.*, 1976; Schilling *et al.*, 1977; Tager *et al.*, 1978). This work was carried out in order to compare the health status of children growing up in a polluted area with that of children in a clean one, taking into account all the above-mentioned factors. It was assumed that children growing up in a region with elevated sulfur dioxide concentrations suffer from more respiratory symptoms and diseases as compared with children growing up in a clean area.

#### MATERIALS AND METHODS

This survey was carried out among schoolchildren from two communities located along the Israeli coast 80 km from each other, but differentially exposed to air pollution. One group lives in Ashdod (Fig. 1), which is an industrialized town, mainly polluted by an 1100-MW oil-fired power station, refineries, and a complex industrial zone (which includes a herbicide factory and acrylic fiber and lead-melting plants). The population of this area numbers about 65,000 (the country of origin of their fathers: 32%, Europe-America: 49%, North Africa: 14%, Asia: and 5%, Israel). The second group lives in Hadera, which was an unpolluted area in 1980 (when this survey was carried out). These baseline health data in Hadera were gathered in the framework of a prospective epidemiological monitoring program carried out in this area since a new 1400-MW coal-fired power plant was to begin operating there in 1982 (Toeplitz *et al.*, 1984). The population of this area numbers about 76,000 persons (the country of origin of their fathers: 39%, Europe-America: 28%, North Africa: 19%, Asia: and 14%, Israel).

**Study population.** Second and fifth grade pupils from 24 schools in Hadera and surroundings (a low-pollution area) were studied in 1980. In 1982 second and fifth grade pupils from 15 schools in Ashdod and surroundings (a polluted area) were surveyed.

**Health questionnaire.** The health questionnaire (Ferris, 1978b) used in this study is a translation into Hebrew of the ATS-NHLI (American Thoracic Society and the National Heart and Lung Institute) health questionnaire to be self-administered by the children's parents. The questionnaires were distributed in both communities between March and June by the school nurse, who also collected them after they had been filled out. From the health questionnaires the following information was obtained: respiratory symptoms and diseases of the children, socioeconomic status, type of household fuel used, smoking habits of the parents, respiratory problems in the families.

Of the 1984 questionnaires distributed in the Hadera area, 1702 were returned—a response rate of 85.8%. In Ashdod, 1826 questionnaires were distributed and 1672 were filled out—a response rate of 91.6%. In both areas, almost all the

2023379777

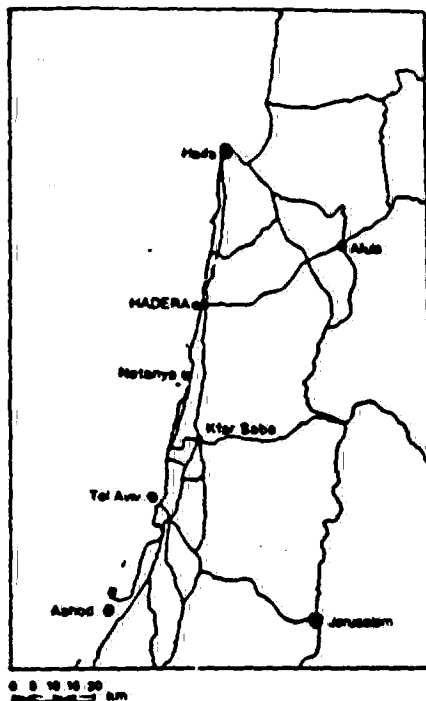


FIG. 1. Site of the two communities Hadera (nonpolluted) and Ashdod (polluted).

children of the studied cohorts living in the community for at least 5 years were examined.

**Air pollution measurements.** Air pollution measurements are carried out in the Hadera area by the local municipal authorities and in the Ashdod area by the electric company. The monitoring stations in the Hadera area (low pollution) are fully automatic and measure  $\text{SO}_2$ ,  $\text{NO}$ ,  $\text{NO}_2$ ,  $\text{NO}_x$ , total hydrocarbons,  $\text{O}_3$ ,  $\text{CO}$ , TSP, and various atmospheric parameters (such as temperature and humidity).  $\text{SO}_2$  is measured by means of a flame photometric instrument, and  $\text{NO}_x$  by a chemiluminescent apparatus.

The monitoring stations in the Ashdod area (polluted) are automatic and measure  $\text{SO}_2$ ,  $\text{NO}_x$ , soiling index, and meteorological parameters.  $\text{SO}_2$  is measured by means of a conductometric instrument and  $\text{NO}_x$  by a chemiluminescent apparatus.

**Analytic procedure.** Statistical analysis of the data was carried out by means of the SPSS program (Nie *et al.*, 1975). Prevalence of respiratory symptoms and diseases according to place of residence was analyzed by means of the  $\chi^2$  test for examination of independence between two variables. The possible effect of a different distribution of background variables in both areas of residence was examined by stratification.

In order to examine the combined effect of all variables in each area, a non-

2023379778

hierarchical logistic model (Dixon *et al.*, 1981) was fitted for the frequency of each respiratory symptom or disease. Those background variables which were included in the logistic regression for each population and the areas of residence were included in the logistic model fitted for the respiratory condition in the pooled data set of both populations. The equation for the predicted proportion of the respiratory condition  $E(f)$  according to the logistic regression is  $E(f) = e^{\alpha} / (1 + e^{\alpha})$  in which  $f$  is the frequency of the respiratory condition,  $n$  is the sample size,  $\alpha = \alpha + \beta_1 x_1 + \beta_2 x_2 + \dots + \beta_m x_m$ , in which  $x_1, x_2, \dots, x_m$  are the background (binary) variables and  $\alpha, \beta_1, \beta_2, \dots, \beta_m$  are the coefficients.

The logistic regression estimates the coefficients of the background variables (such as father's country of origin, crowding index, type of household fuel used, smoking habits of parents, and respiratory diseases among children's fathers) in a stepwise manner.

The relative risk (RR) to suffer from a respiratory condition in the polluted community as compared with the low-pollution community was calculated from the logistic regression as follows:  $RR = e^{\beta_1}$  where  $\beta_1$  is the coefficient of the area of residence.

## RESULTS

SO<sub>2</sub> concentrations—both monthly averages and maximal half-hourly concentrations—are much higher in Ashdod than in Hadera. The same holds for NO<sub>x</sub> concentrations in both areas (Table 1).

The frequency of reported respiratory symptoms (Fig. 2) among schoolchildren from Ashdod, the polluted area, is higher than among children growing up in the

TABLE I  
MONTHLY AVERAGES AND MAXIMAL HALF-HOURLY CONCENTRATIONS OF SULFUR DIOXIDES (IN  $\mu\text{g m}^{-3}$ ) AND NO<sub>x</sub> (IN ppb) IN ASHDOD (POLLUTED AREA) AND IN HADERA (LOW POLLUTED AREA) IN 1982

Month	Hadera				Ashdod			
	SO <sub>2</sub> ( $\mu\text{g m}^{-3}$ )		NO <sub>x</sub> (ppb)		SO <sub>2</sub> ( $\mu\text{g m}^{-3}$ )		NO <sub>x</sub> (ppb)	
	Monthly average	Maximal ½ hr	Monthly average	Maximal ½ hr	Monthly average	Maximal ½ hr	Monthly average	Maximal ½ hr
January	7.0	416	7.7	53	27.7	276	32.3	528
February	7.0	99	6.9	37	42.4	402	7.7*	38
March	6.5	179	8.4	76	22.7	493	13.3	43
April	6.2	146	8.2	57	40.6	670	19.8	127
May	5.2*	169	10.2*	94	45.2	836	32.3	176
June	3.1	135	8.0	95	18.1	415	7.9	69
July	2.6	68	7.3	128	10.6	309	11.3	76
August	1.0	18	6.4	60	18.1	133	11.6	97
September	4.7	140	7.5	64	21.1	417	19.3	63
October	3.4*	166	6.2*	39	28.6	451	17.6	74
November	2.1*	203	6.9*	71	33.0	295	14.8*	78
December	1.8	62	7.0	48	30.4	595	33.3*	200

\* Data availability less than 50%.

2023379779

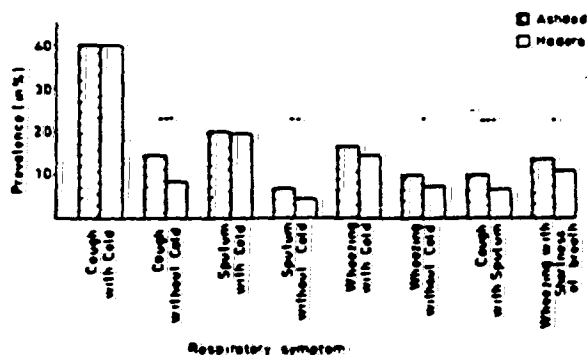


FIG. 2. Prevalence of respiratory symptoms (in %) among second and fifth grade school children from Ashdod (polluted area) and from Hadera (nonpolluted area). \* $P < 0.05$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ .

nonpolluted area (Hadera). Cough without cold, sputum without cold, wheezing without cold, attacks of cough with sputum, and wheezing accompanied by shortness of breath are significantly more common among Ashdod children. It should be emphasized that transient respiratory symptoms, namely, cough with cold, sputum with cold, and wheezing with cold, are not significantly more common among children from the polluted area.

Figure 3 summarizes the frequency of reported respiratory diseases (in %) in second and fifth grade schoolchildren in Ashdod and Hadera. Chest illnesses that kept children from their usual activities, chest illnesses with sputum production, number of such illnesses, pneumonia, bronchitis, and asthma are significantly more prevalent among children growing up in Ashdod. On the other hand, illnesses such as measles, sinus trouble, ear infections and allergy are not significantly more common among Ashdod children. Analysis of background variables which may influence the prevalence of respiratory conditions of the children shows that children in Ashdod grow up in more crowded homes, in fewer houses

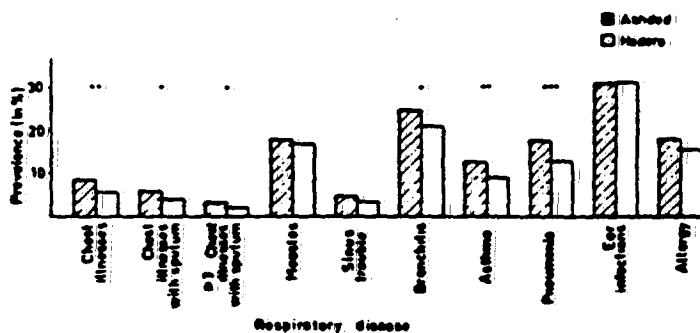


FIG. 3. Prevalence of respiratory diseases (in %) among second and fifth grade school children from Ashdod (polluted area) and from Hadera (nonpolluted area). \* $P < 0.05$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ .

2023379780

with heat, their fathers report more respiratory problems, and their fathers are more frequently from oriental countries, as compared with children from Hadera (Table 2). The effect of these background variables on the prevalence of respiratory problems among Ashdod children was controlled for in further analytic procedures.

It could be shown, by stratification, that the different prevalence of respiratory symptoms and diseases among children from Ashdod and Hadera remains consistent (although not always statistically significant) within the subgroups of background variables. For instance, among children whose houses are heated (Table 3), the prevalence of respiratory symptoms and diseases is higher in Ashdod children than in Hadera children; the difference is statistically significant for most symptoms and diseases.

The logistic models fitted for the respiratory conditions which differed significantly between both areas of residence enabled a calculation of the relative risk to suffer from a respiratory condition in Ashdod as compared with Hadera. Most of the models fitted included the area of residence as a significant component (Table 4). All the models included some background variables, especially respiratory conditions of the fathers.

Most of the models fitted for respiratory conditions demonstrate well the interactions between the respiratory conditions and the background variables.

The relative risks calculated for respiratory conditions in Ashdod are between 1.47 for cough without cold and 2.66 for asthma, as compared with 1.00 for Hadera children.

### DISCUSSION

Our results are in accord with findings in the literature, which indicates a higher prevalence of respiratory symptoms and diseases among children growing up in polluted as compared with nonpolluted areas. The WHO collaborative study on the relationship between air pollution and respiratory diseases in chil-

TABLE 2  
FREQUENCY (IN %) OF BACKGROUND VARIABLES AMONG SECOND AND FIFTH GRADE  
SCHOOLCHILDREN FROM ASHDOD (POLLUTED AREA) AND HADERA (NONPOLLUTED AREA)

Background variable	Frequency in Hadera (%)	Frequency in Ashdod (%)	P value
Crowding index ( $\geq 1.5$ persons/room)	56.0 (1738)*	61.3 (1368)	0.003
No heating	12.6 (1791)	24.0 (1450)	<0.001
Father's education ( $\leq 8$ years)	29.7 (1682)	27.3 (1304)	N.S. (0.168)*
Mother smoking	21.6 (1744)	16.1 (1391)	<0.001
Respiratory diseases among fathers	8.3 (1557)	10.8 (1162)	0.034
Oriental origin of father	52.5 (1775)	68.2 (1420)	<0.001

\* Number of children in parentheses.

\*  $P > 0.05$  is considered as N.S.

2023379781

TABLE 3  
PREVALENCE (IN %) OF RESPIRATORY SYMPTOMS AND DISEASES AMONG SECOND AND FIFTH GRADE SCHOOLCHILDREN FROM ASHDOD (POLLUTED AREA) AND HADERA (NONPOLLUTED AREA) WITHIN THE SUBGROUP OF CHILDREN WHOSE HOUSES ARE HEATED

Respiratory symptom or disease	Prevalence in Hadera (%)	Prevalence in Ashdod (%)	P value
Cough with cold	39.9 (1536)*	40.1 (1080)	N.S. (0.957)*
Cough without cold	8.2 (1530)	14.8 (1075)	<0.001
Sputum with cold	19.1 (1485)	20.8 (1050)	N.S. (0.333)
Sputum without cold	3.9 (1481)	6.9 (1038)	0.001
Wheezing with cold	14.0 (1426)	17.0 (997)	0.050
Wheezing without cold	7.1 (1245)	9.8 (936)	0.030
Cough + sputum	6.3 (1423)	10.1 (1009)	<0.001
Wheezing with shortness of breath	10.6 (1467)	13.6 (1029)	0.028
Chest illnesses	5.8 (1509)	9.5 (1051)	<0.001
Chest illness with sputum	4.5 (1398)	7.8 (1020)	<0.001
Three or more illnesses with sputum	2.4 (1404)	4.5 (1006)	0.005
Measles	16.4 (1292)	17.5 (888)	N.S. (0.560)
Sinus trouble	4.9 (1248)	3.7 (859)	N.S. (0.243)
Bronchitis	22.0 (1325)	25.4 (903)	N.S. (0.070)
Asthma	9.8 (1261)	13.0 (868)	0.026
Pneumonia	12.9 (1307)	18.1 (901)	0.001
Ear infections	31.7 (1304)	32.6 (868)	N.S. (0.683)
Allergy	15.9 (1493)	19.1 (1018)	0.043

\* Number of children in parentheses.

\*  $P > 0.05$  is considered as N.S.

dren (Colley and Brasser, 1980) showed a close association between air pollution and various respiratory indices in children. The Groupe Cooperatif PAARC (1982) also demonstrated that children growing up in  $SO_2$ -polluted areas in France show a higher prevalence of upper respiratory symptoms.

TABLE 4  
RELATIVE RISK FOR RESPIRATORY SYMPTOMS AND DISEASES FOR SECOND AND FIFTH GRADE SCHOOLCHILDREN FROM ASHDOD (POLLUTED AREA) AS COMPARED TO HADERA (NONPOLLUTED AREA)

Respiratory symptom or disease	Hadera	Ashdod	P value (for area)
Cough without cold	1.00	1.47	0.049
Cough + sputum*	1.00	1.55	0.007
Chest illnesses	1.00	1.95	0.003
Chest illnesses + sputum	1.00	1.91	0.015
Bronchitis*	1.00	2.30	0.008
Asthma	1.00	2.66	0.039
Pneumonia	1.00	1.47	0.003
Respiratory diseases among siblings	1.00	1.54	0.002

\* The model does not fit very well ( $P$  value for model  $< 0.1$ ).

2023379782

Other cross-sectional surveys carried out among schoolchildren in different countries also showed an association between area of residence and prevalence of upper and lower respiratory tract illnesses (Colley and Holland, 1967; French *et al.*, 1973; Hammer *et al.*, 1976; Love *et al.*, 1981; Lunn *et al.*, 1967; Melia *et al.*, 1981; Mostardi *et al.*, 1981b; Toyama, 1964).

Ferris (1978a), in a review article, criticized most children studies, especially because of insufficient control of possible confounding factors, and because exposures for children were only estimated.

Lebowitz (1981) recommends spatiotemporal designs as useful strategies in surveillance of respiratory effects of point sources of pollution. In this study, we tried to estimate health effects in two communities with different pollution levels. We used a spatial approach in which multivariate statistical analyses were performed in order to control for possible confounding factors. As in other environmental studies, only estimates of exposure for children, based on community monitoring, were available.

Monthly average concentrations of  $\text{SO}_2$  in Ashdod are within the range of 10.6 and 45.2  $\mu\text{g}/\text{m}^3$ , with an annual average of about 30  $\mu\text{g}/\text{m}^3$ .

In their study, Love *et al.* (1981) demonstrated health effects among schoolchildren with air pollution levels similar to those measured in our study. Melia *et al.* (1981) could not show any relation between prevalence of respiratory illness and  $\text{SO}_2$  annual means ranging from 12 to 114  $\mu\text{g}/\text{m}^3$ . Other studies (French *et al.*, 1973; Groupe Cooperatif PAARC, 1982; Hammer *et al.*, 1976; Mostardi *et al.*, 1981b) indicate higher  $\text{SO}_2$  concentrations as threshold levels for aggravation of respiratory conditions.

It is possible that other pollutants, either separately or in combination with  $\text{SO}_2$  and  $\text{NO}_x$ , contribute to the observed health effects. Since no measurements of the concentrations of heavy metals and organics (herbicides, for example) are carried out in Ashdod, their contribution to the health status of the population is not known.

In our survey, we could show that chronic respiratory symptoms, and most pulmonary diseases, were significantly more common among children from the polluted area. The higher prevalence of only the chronic (and not the transient) respiratory symptoms can not be attributed to general tendency of the population in Ashdod to overreport respiratory conditions among their children.

It is of interest that the logistic models fitted for the respiratory conditions better demonstrate the interaction between the background variables and the respiratory diseases, rather than the interaction with respiratory symptoms. The relative risks calculated for respiratory symptoms in Ashdod children were found to be about 1.50, and those for pulmonary diseases within the range of 1.47 and 2.66, as compared with 1.00 for Hadera children.

#### REFERENCES

- Biersteker, K., and van Leeuwen, P. (1970). Air pollution and peak flow rates of schoolchildren in two districts of Rotterdam. *Arch. Environ. Health* 20, 382-384.
- Bland, M., Bewley, B. R., Pollard, V., and Banks, M. H. (1978). Effect of children's and parents' smoking on respiratory symptoms. *Arch. Dis. Children* 53, 100-105.

2023379783

- Cameron, P., Kostin, J. S., Zaks, J. M., Wolfe, J. H., Tighe, G., Oselett, B., Stocker, R., and Winton, J. (1969). The health of smokers' and non-smokers' children. *J. Allergy* 43, 336-341.
- Colley, J. R. T., and Holland, W. W. (1967). Social and environmental factors in respiratory disease. *Arch. Environ. Health* 14, 157-161.
- Colley, J. R. T., and Reid, D. D. (1970). Urban and social origins of childhood bronchitis in England and Wales. *Brit. Med. J.* 2, 213-217.
- Colley, J. R. T., Douglas, J. W. B., and Reid, D. D. (1973). Respiratory disease in young adults: Influence of early childhood. *Brit. Med. J.* 2, 195-198.
- Colley, J. R. T. (1974). Respiratory symptoms in children and parental smoking and phlegm production. *Brit. Med. J.* 2, 201-204.
- Colley, J. R. T., and Brasser, L. J. (1980). "Chronic Respiratory Diseases in Children in Relation to Air Pollution: Report on WHO Study Euro Reports and Studies 28. Copenhagen.
- Dixon, W. J., Brown, M. B., Engelman, L., France, J. W., Hill, M. A., Jennrich, R. I., and Toporek, J. D. (1981). "BMDP Statistical Software." Univ. of California Press, Berkeley.
- Fergusson, D. M., Horwood, L. J., and Shannon, F. T. (1980). Parental smoking and respiratory illness in infancy. *Arch. Dis. Children* 55, 358-361.
- Fergusson, D. M., Horwood, L. J., Shannon, F. T., and Taylor, B. (1981). Parental smoking and lower respiratory illness in the first three years of life. *J. Epidem. Commun. Health* 35, 180-184.
- Ferris, B. G. (1978a). Health effects of exposure to low levels of regulated air pollutants—A critical review. *JAPCA* 28, 482-497.
- Ferris, B. G. (1978b). Epidemiology Standardization Project. *Amer. Rev. Resp. Dis.* 118, 1-120.
- French, J. G., Lowrimore, G., Nelson, W. C., Finklea, J. F., English, T., and Hertz, M. (1973). The effect of sulfur dioxide and suspended sulfates on acute respiratory disease. *Arch. Environ. Health* 27, 129-133.
- Goldsmith, J. R., and Friberg, L. T. (1977). Effects of air pollution on human health. In "Air Pollution" (A. C. Stern, Ed.), Vol. 1, 3rd ed., pp. 458-610. Academic Press, New York.
- Goren, A. I., and Goldsmith, J. R. (1986). Epidemiology of childhood respiratory disease in Israel. *Eur. J. Epidemiol.* 2, 139-150.
- Groupe Cooperatif PAARC (1982). Pollution atmospherique et affections respiratoires chroniques ou à répétition: II. Resultats et discussion. *Bull. Eur. Physiopathol. Resp.* 18, 101-116.
- Hammer, D. I., Miller, F. J., Stead, A. G., and Hayes, C. G. (1976). Air pollution and childhood lower respiratory disease. I. Exposure to sulfur oxides and particulate matter in New York, 1972. In "Clinical Implications of Air Pollution Research", pp. 321-337. Publishing Sciences Group, Acton, MA.
- Hasselblad, V., Humble, C. G., Graham, M. G., and Anderson, H. S. (1981). Indoor environmental determinants of lung function in children. *Amer. Rev. Resp. Dis.* 123, 479-485.
- Higgins, M., and Keller, J. (1975). Familial occurrence of chronic respiratory disease and familial resemblance in ventilatory capacity. *J. Chron. Dis.* 28, 239-251.
- Holland, W. W., Kasap, H. S., Colley, J. R. T., and Cormack, W. (1969a). Respiratory symptoms and ventilatory function: A family study. *Brit. J. Prev. Soc. Med.* 23, 77-84.
- Holland, W. W., Halil, T., Bennett, A. E., and Elliott, A. (1969b). Factors influencing the onset of chronic respiratory disease. *Brit. Med. J.* 2, 205-208.
- Holma, B., Kjaer, G., and Stokholm, J. (1979). Air pollution, hygiene and health of the Danish schoolchildren. *Sci. Total Environ.* 12, 251-286.
- Irvine, D., Brooks, A., and Waller, R. (1980). The role of air pollution, smoking and respiratory illness in childhood in the development of chronic bronchitis. *Chest* 77, 251-253.
- Lebowitz, M. D., and Burrows, B. (1976). Respiratory symptoms related to smoking habits of family adults. *Chest* 69, 48-50.
- Lebowitz, M. D. (1981). Respiratory indicators. *Environ. Res.* 25, 225-235.
- Leeder, S. R., Corkhill, R. T., Irwig, L. M., Holland, W. W., and Colley, J. R. T. (1976). Influence of family factors on the incidence of lower respiratory illness during the first year of life. *Brit. J. Prev. Soc. Med.* 30, 203-212.
- Love, G. J., Lan, S. P., Shy, C. M., and Struba, R. J. (1981). The incidence and severity of acute respiratory illness in families exposed to different levels of air pollution. New York metropolitan area, 1971-1972. *Arch. Environ. Health* 36, 66-74.

2023379784



- Lunn, J. E., Knowelden, J., and Handyside, A. J. (1967). Patterns of respiratory illness in Sheffield infants schoolchildren. *Brit. J. Prev. Soc. Med.* 21, 7-16.
- Metia, R. J. W., Florey, C. du V., and Swan, A. V. (1981). Respiratory illness in British schoolchildren and atmospheric smoke and  $\text{SO}_2$ , 1973-1977. I. Cross-sectional findings. *J. Epidem. Commun. Health* 35, 161-167.
- Mostardi, R. A., Ely, D. L., Woebkenberg, N. R., Richardson, B., and Jarrett, M. T. (1981a). The University of Akron Study on Air Pollution and Human Health Effects. I. Methodology, baseline data and aerometrics. *Arch. Environ. Health* 36, 243-249.
- Mostardi, R. A., Woebkenberg, N. R., Ely, D. L., Conlon, M., and Atwood, G. (1981b). The University of Akron Study on Air Pollution and Human Health Effects. II. Effects of acute respiratory illness. *Arch. Environ. Health* 36, 250-255.
- Nie, N. H., Hull, C. H., Jenkins, J. G., Steinbrenner, K., and Bent, D. H. (1975). "SPSS Statistical Package for the Social Sciences." 2nd ed. McGraw-Hill, New York.
- Peat, J. K., Woolcock, A. J., Leeder, S. R., and Blackburn, C. R. (1980). Asthma and bronchitis in Sydney schoolchildren. II. The effect of social factors and smoking on prevalence. *Amer. J. Epidem.* 111, 728-735.
- Schilling, R. S. F., Letai, A. D., Hui, S. L., Beck, G. J., Schoenberg, J. B., and Bouhuys, A. (1977). Lung function, respiratory disease and smoking in families. *Amer. J. Epidem.* 106, 274-283.
- Tager, I., Tishler, P. V., Rosner, B., Speizer, F. E., and Litt, M. (1978). Studies of the familial aggregation of chronic bronchitis and obstructive airways disease. *Intern. J. Epidem.* 7, 55-62.
- Tager, I. R., Weiss, S. T., Rosner, B., and Speizer, F. E. (1979). Effect of parental cigarette smoking on the pulmonary function of children. *Amer. J. Epidem.* 110, 15-26.
- Toeplitz, R., Goren, A., Goldsmith, J. R., and Donagil, A. (1984). Epidemiological monitoring in the vicinity of a coal-fired power plant. *Sci. Total Environ.* 32, 233-246.
- Toyama, T. (1964). Air pollution and its health effects in Japan. *Arch. Environ. Health* 8, 153-173.
- Vedall, S., Schenker, M. B., Samet, J. M., and Speizer, F. E. (1984). Risk factors for childhood respiratory disease. *Amer. Rev. Resp. Dis.* 130, 187-192.
- Ware, J. H., Dockery, D. W., Spiro, A., Speizer, F. E., and Ferris, B. G. (1984). Passive smoking, gas cooking and respiratory health of children living in six cities. *Amer. Rev. Resp. Dis.* 129, 366-374.

2023379785

2023379786

Nordvall, S.L., Eriksson, M., Rylander, E., Schwartz, B.  
"Sensitization of Children in the Stockholm Area to House Dust  
Mites" Acta Paediatrica Scand 77:716-720, 1988.

**ABSTRACT:** Atopic sensitization of children in the Stockholm area to house dust mites (HDM) was investigated in a case-control study. Sixty children with and 60 without positive skin prick tests for HDM were matched for age and sex. HDM-sensitized children had previously more often lived in other areas known to be mite infested than the control children. Sensitization to mites was related to dampness in the homes, but no significant relationship was found to the type of residence, frequent visits to a summer house in the archipelago or parental smoking. Dust samples from mattresses of the children with the strongest positive reactions to mites in skin prick tests and the respective controls were subjected to an enzyme immunoassay, to measure the content of the major allergens of the Dermatophagoids (D.) species *D. pterinyssinus*, *D. farinae* and *D. microceras*. Mattress dust samples from the beds of HDM-sensitized children contained significantly higher HDM antigen concentrations than those from the beds of controls. Private houses contained significantly more HDM antigens than flats and 10 of 11 homes in which a dampness problem was recognized contained mite antigens. It is postulated that mite infestation is increasing in the area, energy-saving measures created improved conditions for HDM survival.

2023379787

## Sensitization of Children in the Stockholm Area to House Dust Mites

S. L. NORDVALL, M. ERIKSSON, E. RYLANDER and B. SCHWARTZ

From the Department of Paediatrics, St. Göran's Children's Hospital, Stockholm, Sweden and Allergologisk Laboratorium, Copenhagen, Denmark

**ABSTRACT.** Nordvall, S. L., Eriksson, M., Rylander, E. and Schwartz, B. (Department of Paediatrics, St. Göran's Children's Hospital, Stockholm, Sweden and Allergologisk Laboratorium, Copenhagen, Denmark). Sensitization of children in the Stockholm area to house dust mites. *Acta Paediatr Scand* 77: 716, 1988.

Atopic sensitization of children in the Stockholm area to house dust mites (HDM) was investigated in a case-control study. Sixty children with and 60 without positive skin prick tests for HDM were matched for age and sex. HDM-sensitized children had previously more often lived in other areas known to be mite infested than the control children. Sensitization to mites was related to dampness in the homes, but no significant relationship was found to the type of residence, frequent visits to a summer house in the archipelago or parental smoking. Dust samples from mattresses of the children with the strongest positive reactions to mites in skin prick tests and the respective controls were subjected to an enzyme immunoassay, to measure the content of the major allergens of the *Dermatophagoides* (*D.*) species *D. pterinysinus*, *D. farinae* and *D. microcerus*. Mattress dust samples from the beds of HDM-sensitized children contained significantly higher HDM antigen concentrations than those from the beds of controls. Private houses contained significantly more HDM antigens than flats and 10 of 11 homes in which a dampness problem was recognized contained mite antigens. It is postulated that mite infestation is increasing in the area, energy-saving measures creating improved conditions for HDM survival. **Key words:** house dust mites, *Dermatophagoides*, allergen analysis, ELISA.

House dust mites of the genus *Dermatophagoides* (HDM) are known to be important allergens in cases of dust allergy (1, 2). The growth and survival of HDM are known to depend on climatic conditions, the most important being the humidity in the homes (2-8). For HDM survival a relative humidity (RH) of 55% is required and the optimal RH for HDM growth is known to be as high as 75-80%. Since climatic conditions thus greatly influence the quantities of HDM in house dust, considerable differences are found between different geographic regions (9, 10), between seasons (11, 12) and also between different houses (7).

The general climatic conditions in the Stockholm area are unfavourable for growth of HDM, the winters being cold, with a prolonged indoor heating season and an indoor RH that is generally much below the critical 55% for HDM survival. In a previous study (13) mite concentrations in house dust from this area were found to be very low and *Dermatophagoides* were virtually absent. Yet in our daily practice we see children who are obviously sensitized to HDM, as shown by positive skin prick tests and radioallergosorbent tests for these allergens. This study was undertaken to find out the causes of sensitization to HDM in our area.

### MATERIAL AND METHODS

The study comprised children who were attending the out-patient allergy clinic of St. Göran's Children's Hospital in 1984-1986 for routine tests. Skin prick tests (SPT) were carried out in accordance with the Nordic guidelines (14); during the period January 1984 to November 1985 Pharmed® 10000 BU (Pharmacia AB, Uppsala, Sweden) was used and from December 1985 onwards the tests were performed with allergen precoated lancets (Phazet®) from the same supplier. The wheal sizes were related to those of histamine hydrochloride 1 mg/ml. A panel of ten allergens was used: *Dermatophagoides pterinysinus* (*D.pt.*), *Dermatophagoides farinae* (*D.f.*), cat., dog., horse, timothy, *Cladosporium her-*

2023379788

barum, *Alternaria alternata*, birch and mugwort. Sixty-six children with a positive SPT reaction (1+ or more, minimal mean wheal size 2.5 mm with a flare) to either or both of the two *Dermatophagoides* species were included in the study. Another 66 children who had been tested during the same time period for suspected allergies but had negative SPT to both *Dermatophagoides* species in SPT served as controls. A total of 80 boys and 52 girls aged 3–17 years were included in the study. Matching was performed with respect to both age and sex.

**Questionnaire.** The parents were asked to complete a questionnaire concerning the children's previous environment, i.e. whether they had lived in mite-infested regions in southern Sweden or abroad. Questions were also asked about paternal and maternal smoking, type of residence—i.e. whether they lived in a private house or a flat—and whether the family frequented a summer house in the Stockholm archipelago. There was also a question as to whether dampness was recognized as a problem in their permanent home. Forms were completed for 60 matched pairs of children.

**Dust sampling.** A mattress dust sample was requested from the beds of those mite-sensitized children who had displayed at least one 3+ SPT reaction to either of the two HDM species or 2+ reactions to both, and also from the beds of the respective controls. Dust from houses where a moisture problem had been acknowledged was also collected. Sampling was performed as described by Mosbech & Lind (15), by the parents, using their usual vacuum cleaner and a specially designed nozzle with a thick filter paper (13). This was done in 1986 from the last week of September to the end of October. Out of 62 requested samples, 54 were obtained and analysed.

**Dust analyses.** Aqueous extracts were prepared as previously described by suspending each gram of the dust sample in 5 cc of 0.9% saline (16). The contents of HDM antigens were determined by an enzyme-linked immunosorbent assay (ELISA), using affinity purified monospecific antisera against the major mite allergens of three *Dermatophagoides* species: *pteronyssinus* (antigen Der pI, formerly Dp 42 or P1), *farinae* (antigen Der fI) and *microceras* (antigen Der mI) (17). Standard Quality HDM extracts from Allergologisk Laboratorium A/S, Copenhagen, Denmark, were used as reference allergen solutions. Standard curves were run simultaneously on each of the plates. Less than 0.1% cross-reactivity was observed between these species-specific antisera in the ELISA assay (17).

**Statistics.** Fisher's exact test was used for comparison of data for cases and controls obtained by the questionnaires. Non-parametric tests were used in the processing of data for dust antigen contents, paired tests for the matched case-control comparisons (Wilcoxon signed ranks test) and the Mann-Whitney test for other comparisons.

## RESULTS

**Questionnaire.** A significantly higher proportion of the children with positive SPT to HDM than of the controls, reported long stays in mite-infested areas abroad or in southern Sweden (Table 1). More mite-sensitized children than control children lived in private houses but this difference was not significant. The parents of mite-sensitized children acknowledged a problem of dampness in their home more frequently than those of the controls ( $p < 0.006$ ). The frequency of visits to a summer house in the archipelago was similar in the two groups. A higher proportion of the mothers of mite-sensitized children than of control children were smokers, but this difference was not significant ( $p < 0.16$ ).

Table 1. Data on environmental factors obtained from questionnaire

	Travel		Private house		Dampness in home		Summer-house		Mother smoker		Father smoker	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Case	32	21	28	29	11	46	12	45	22	35	12	44
Control	17	39	22	38	2	58	17	43	17	43	18	41
<i>p</i> values	<0.003		<0.12		<0.006		<0.24		<0.16		<0.18	

Cases (mite-sensitized children) compared with controls (children without sensitization to mites). Statistics: Fisher's exact test. Travel=children with and without frequent stays in southern Sweden or other mite-infested areas.

2023379789

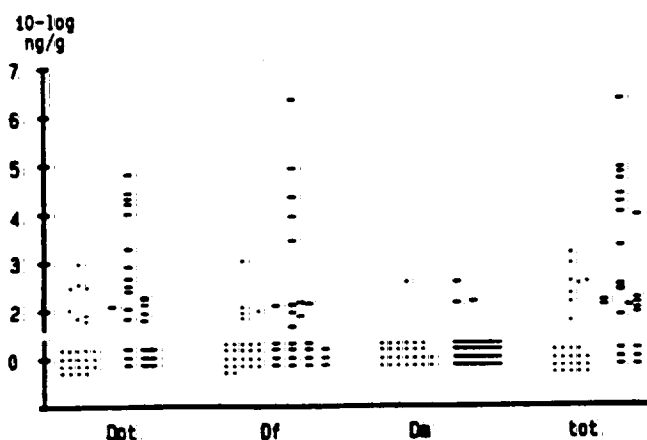


Fig. 1. House dust mite antigen contents from beds of mite-sensitized children (•) and controls (○). Dpt, Df and Dm = contents of antigens Der pI, Der fI and Der mI, respectively. tot = total amount of the three *Dermaophagoides* antigens.

**Dust analyses.** HDM antigens Der pI and Der fI were found in a considerable proportion of the dust samples, whereas antigen Der mI was found only sparsely. Dust from the homes of mite-sensitized children contained larger total amounts of mite antigens than dust from the homes of controls (Fig. 1) ( $p < 0.001$ ). This difference was significant both for Der pI ( $p < 0.02$ ) and for Der fI ( $p < 0.03$ ). The difference in mite antigen contents between private houses and flats (Fig. 2) was striking and was significant both for the total mite antigen contents ( $p < 0.001$ ) and for Der pI ( $p < 0.005$ ) and Der fI ( $p < 0.02$ ). A high proportion (10 of 11) of the dust samples obtained from houses where a dampness problem was recognized contained HDM antigens (Fig. 3).

## DISCUSSION

From the results of this study two explanations emerge for the mite-sensitization observed among children in a Stockholm allergy clinic. One of them is obvious, i.e. previous residence in or frequent visits to other more heavily mite infested areas. The most important cause of the sensitization of the children, however, was the occurrence of HDM antigens in

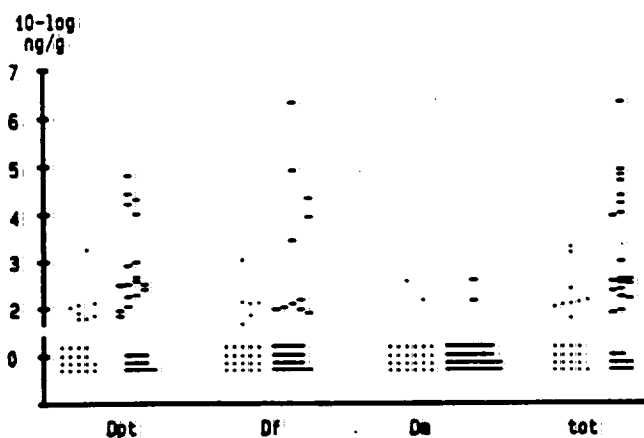
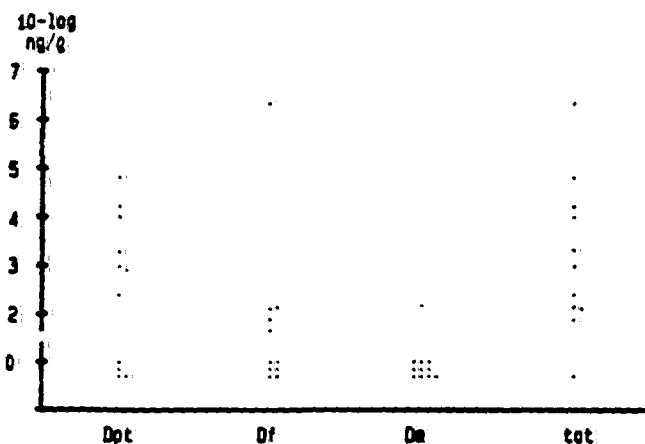


Fig. 2. House dust mite antigen contents from private houses (•) and flats (○). For further explanations, see legend to Fig. 1.

2023379790



**Fig. 3. House dust mite antigen contents in homes with acknowledged dampness problems. For further explanations, see legend to Fig. 1.**

In a previous study (13) *Dermatophagoides* were found to be very rare in the homes of the area. There may be several explanations for the divergent results of these two studies. In the previous study dust was collected from the homes of adults. A correlation between mite-sensitization in adults and the presence of HDM in their current homes is not expected to the same degree as in children, since adults are more likely to have been sensitized elsewhere and at a younger age. Further, in Türos' study (13) dust was collected all through the year, whereas our samples were collected in the autumn, when peak levels could be anticipated. Microscopy was used in Türos' study for the detection and quantification of mites, whereas we used a modern ELISA technique. These two techniques are not known to differ, however, when properly performed (17). Even though some differences in the design of the two studies may thus partly explain the discrepant results, it appears probable, that the difference reflects a true increase in HDM infestation in the area.

Increased mite infestation is a possible consequence of the changes in the construction of buildings that resulted from the energy crisis in the early seventies. Improved insulation and decreased ventilation of homes may have created a more favourable indoor climate for mite survival. Many homes in Sweden that were constructed in the late seventies smell of mould, but this problem occurs only rarely in older buildings and then often in conjunction with renovations (18). These findings are in accordance with the hypothesis that mite infestation of homes has increased and that the consequent sensitization to mites and clinical mite allergy may be of increasing importance in our area. Our findings, that private houses are more prone to mite infestation than flats, and the observed and very likely relation to problems of dampness, add further support to this notion.

In a majority of the dust samples HDM antigens were not detectable by the ELISA technique. This contrasts with findings from Copenhagen, where only a minority of the houses were found to be free of HDM antigens, when the same ELISA technique was used to examine dust from unselected houses (17). The general climatic conditions are probably more favourable for mite growth in Denmark than in our area, where the indoor climate possibly has a greater impact. In Denmark too, however, there are considerable discrepancies in the concentrations of HDM in house dust between different houses (7, 17), which has been attributed in part to differences in housing conditions (7).

The spread of HDM to houses of our temperate regions, where the general climatic con-

2023379791

ditions are unfavourable for mite growth, deserves further attention. Technical investigations of the types of houses that are associated with these problems seem important from a preventive aspect. Those who have already encountered this problem in their homes need technical advice to help them to eliminate mites. Studies performed in other regions of the world do not necessarily apply to our local conditions, and effects of improved ventilation and other measures for HDM sanitation should also be evaluated here.

#### ACKNOWLEDGEMENTS

This study was supported by the Research Funds of the Karolinska Institute. Sig-Britt Spång is gratefully acknowledged for administering the study.

#### REFERENCES

1. Berrens L. The allergens of house dust. *Prog Allergy* 1970; 14: 259-339.
2. Voorhorst R, Spieksma FTM, Varekamp H, Leupen MJ, Lyklema AW. The house-dust mite (*Dermaphagoides pteronyssinus*) and the allergens it produces. Identity with the house dust allergen. *J Allergy* 1967; 39: 325-39.
3. Burr ML, Dean BV, Merret TG, Neale E, St Leger AS, Verrier-Jones ER. Effects of anti-mite measures on children with mite sensitive asthma: a controlled trial. *Thorax* 1980; 35: 506-12.
4. Dobson RM. Some effects of microclimate on the longevity and development of *Dermaphagoides pteronyssinus* (Trouessart). *Acarologia* 1979; 21: 482-86.
5. Koekkoek HHM, van Bronswijk JEMH. Temperature requirements of a house-dust mite *Dermaphagoides pteronyssinus* compared with the climate in different habitats of houses. *Entomol Exp Appl* 1972; 15: 438-42.
6. Korsgaard J. Preventive measures in mite asthma. A controlled trial. *Allergy* 1983; 38: 93-102.
7. Korsgaard J. Mite asthma and residency. A case-control study on the impact of exposure to house-dust mites in dwellings. *Am Rev Respir Dis* 1983; 128: 231-35.
8. Mosbech H. House dust mite allergy. *Allergy* 1985; 40: 81-91.
9. Green WF, Sedgwick C, Woolcock AJ, Leeder SR, Stuckey M. House dust mites and skin tests in different Australian localities. *Aust NZ J Med* 1986; 16: 639-43.
10. Murray AB, Fergusson AC, Morrison BJ. Sensitization to house dust mites in different climatic areas. *J Allergy Clin Immunol* 1985; 76: 108-12.
11. Arlian LG, Bernstein IL, Gallagher JS. The prevalence of house dust mites, *Dermaphagoides* spp., and associated environmental conditions in homes in Ohio. *J Allergy Clin Immunol* 1982; 69: 527-32.
12. Hallas TE, Korsgaard J. Annual fluctuations of mites and fungi in Danish house-dust: An example. *Allergol Immunopathol* 1983; 11: 195-200.
13. Tuross M. Mites in house dust in the Stockholm area. *Allergy* 1979; 34: 11-18.
14. Aas K, Belin L. Standardization of diagnostic work in allergy. *Acta Allergol* 1974; 29: 239-40.
15. Mosbech H, Lind P. Collection of house dust for analysis of mite allergens. *Allergy* 1986; 41: 373-78.
16. Schwartz B, Gravesen S, Petersen BN, Weeke ER. Laboratory investigations for allergens in the home. *Ugeskr Laeger* 1979; 141: 882-86.
17. Lind P. Enzyme-linked immunosorbent assay for determination of major excrement allergens of house dust mite species *D. pteronyssinus*, *D. farinae* and *D. microceras*. *Allergy* 1986; 41: 442-51.
18. Samuelsson I. Sick houses—a problem of moisture. In: Berglund B, Lindvall T, Sundell J, eds. *Indoor air*. Stockholm: Swedish Council for Building Research, 1984; Vol 1: 341-46.

Submitted June 6, 1987. Accepted March 11, 1988

(S. L. N.): Department of Paediatrics  
S:t Göran's Hospital  
S-11281 Stockholm  
Sweden

2023379792



2023379793

Mitchell, E.A., Stewart, A.W., Pattemore, P.K., Asher, M.I., Harrison, A.C., Rea, H.H. "Socioeconomic Status in Childhood Asthma", International Journal of Epidemiology 18(4): 888-890, 1989.

SUMMARY: This study examines the relationship between socioeconomic status (SES) and asthma prevalence and the use of asthma medication. One thousand and fifty European children aged eight and nine years were studied by parent completed questionnaire and histamine inhalation challenge. After controlling for sex of the child and for smokers in the house there were significantly higher lifetime ( $P = 0.029$ ) and current ( $P = 0.046$ ) prevalence rates of wheeze in children in low SES groups. There was no relationship between SES and asthma diagnosis, bronchial hyperresponsiveness (BHR:  $PD_{20} < 7.8 \mu\text{mol}$ ), or any combination of BHR with symptoms or diagnosis.

The use of bronchodilators and asthma prophylactic drugs was less frequent in the low SES groups of children with wheeze in the last 12 months both with concurrent BHR or irrespective of BHR than in those in high SES groups.

2023379794

# Socioeconomic Status in Childhood Asthma

EDWIN A MITCHELL, ALISTAIR W STEWART, PHILIP K PATTEMORE, M INNES ASHER,  
ADRIAN C HARRISON AND HAROLD H REA

Mitchell E A (Department of Pediatrics, School of Medicine, University of Auckland, Private Bag, Auckland, New Zealand), Stewart A W, Pattemore P K, Innes Asher M, Harrison A C and Rea H H. Socioeconomic status in childhood asthma. *International Journal of Epidemiology* 1989, 18: 888-890.

This study examines the relationship between socioeconomic status (SES) and asthma prevalence and the use of asthma medication. One thousand and fifty European children aged eight and nine years were studied by parent completed questionnaire and histamine inhalation challenge. After controlling for sex of the child and for smokers in the house there were significantly higher lifetime ( $P = 0.029$ ) and current ( $P = 0.046$ ) prevalence rates of wheeze in children in low SES groups. There was no relationship between SES and asthma diagnosis, bronchial hyperresponsiveness (BHR: PD20  $< 7.8 \mu\text{mol}$ ), or any combination of BHR with symptoms or diagnosis.

The use of bronchodilators and asthma prophylactic drugs was less frequent in the low SES groups of children with wheeze in the last 12 months both with concurrent BHR or irrespective of BHR than in those in high SES groups.

For many diseases poor health is both more prevalent and more severe in children in families with low socioeconomic status (SES) than in children from better circumstances.<sup>1</sup> While some studies suggest that there is an excess of severe asthma in children with low SES,<sup>2,3</sup> several studies have suggested that there is a higher prevalence of asthma in children in high SES families compared with those in low SES,<sup>3,5</sup> and other studies have not found any relationship between asthma prevalence and SES.<sup>6,9</sup>

During a study comparing asthma prevalence between Australian and New Zealand schoolchildren<sup>10</sup> we have had the opportunity to examine the relationship between SES and the prevalence of childhood asthma using a number of different criteria for asthma (including bronchial hyperresponsiveness (BHR)) and the use of asthma medications. This study is reported here.

## METHODS

The methodology has been described in detail elsewhere.<sup>10</sup> Briefly a random sample of approximately 1 300 European children was selected from the Auckland region.

A questionnaire was completed by the parents, which included questions about demographic details of the child and parents, a history of asthma symptoms, diagnosis, current medications for asthma, and parental or other household members' smoking habits. The children underwent a histamine inhalation challenge using the method of Yan *et al.*<sup>11</sup> Children whose forced expiratory volume in one second (FEV<sub>1</sub>) fell by more than 20% of baseline after receiving a cumulative dose of 7.8  $\mu\text{mol}$ s histamine or less were considered to have bronchial hyperresponsiveness (BHR). Socioeconomic status was defined from a revision of the Elley Irving socioeconomic six-point index for New Zealand occupations using the father's present or most recent occupation if he lived at home, otherwise the mother's occupation.<sup>12</sup> Five groupings were used (1-5) with group one representing the highest level and group five representing indices 5 and 6 combined.

Seven criteria for asthma prevalence were used for comparison with SES: any wheeze (including exercise wheeze) ever, any wheeze in the last 12 months and asthma diagnosed ever. The number of children with concomitant BHR in each category was also assessed. The seventh criteria was the presence or absence of BHR overall.

The current use of bronchodilators and asthma prophylactic drugs (inhaled steroids, cromoglycate) were examined by SES group in children with wheeze in the

Departments of Paediatrics and Community Health, School of Medicine, University of Auckland and the Department of Respiratory Medicine, Greenlane Hospital, Auckland.

Reprint requests: Dr E A Mitchell, Department of Paediatrics, School of Medicine, University of Auckland, Private Bag, Auckland 1, New Zealand

last 12 months, both with concurrent BHR or irrespective of BHR. Because of small numbers SES groups 1-2 and 4-6 were combined for this analysis.

The effect of the socioeconomic status of the children on the various measures of asthma was assessed by use of a logistic regression model. As it was thought that the smoking status of members of the household and the child's sex may have some confounding influence, these variables were also included in the model. Each of the asthma measures used were in the two category form, present or absent. Smoking was also classified as presence or absence of maternal smoker, paternal smoker or any smoker living in the household. The hypothesis considered was that there was a linear trend in the proportion of children with a positive outcome over the socioeconomic categories. With the size of sample available the power to detect an increase of 3.5% in outcome for each step from the highest socioeconomic category to the lowest was approximately 65 to 75%.

## RESULTS

Of those sampled (84%) 1084 children were tested. SES could not be ascertained from the questionnaires in 34 children, leaving a final sample size of 1050.

Table 1 gives the crude prevalence rates for the five SES groups for the seven chosen asthma criteria and the probability (*p*) for a linear trend in SES after controlling for any smokers in the house and for sex of the child. A similar pattern of results is obtained regardless of whether the smoking variable being controlled for is mother's smoking, father's smoking or any smoker in the house. The lifetime or current prevalence rates for any wheeze (including exercise wheeze) are significantly higher in lower SES groups ( $p = 0.029$  and  $p = 0.046$  respectively), whereas there is no relationship between SES and the diagnosis of asthma, BHR or any combination of BHR with symptoms and previous asthma diagnosis.

Table 2 shows the prevalence of asthma medication use by SES group in asthmatic children using the criteria for asthma which include wheeze in the last 12 months. There is a clear trend for greater use of asthma medications in higher SES groups and this is particularly notable for prophylactic drugs.

## DISCUSSION

SES can be measured in a number of ways, the commonest being occupation, education or income. In other studies examining the relationship between SES and asthma prevalence the results have tended to be consistent irrespective of the measure of SES used. This study used occupation as the measure of SES.

The definition of asthma in previous studies has depended upon questionnaires and frequently upon parental reporting of asthma. In this study the parental questionnaire also sought information about wheezing, and the children were tested for BHR. The relationship between these factors and the diagnostic label 'asthma' is not straightforward. Furthermore, it is well established that asthma may be underdiagnosed.<sup>11</sup> Thus studies which have related asthma diagnosis to SES may yield different results from comparisons of symptoms and/or BHR to SES.

The higher prevalence of asthma diagnosis in high SES groups seen in earlier studies may reflect a SES effect on the disease label rather than the disease itself. This and other recent studies<sup>7,8</sup> have found no relationship between SES and asthma diagnosis, suggesting there may have been a change in the use of the label with time.

Studies defining asthma by wheezy symptoms have tended to find no relationship with SES.<sup>8,9</sup> In contrast this study found significantly higher rates of wheezy symptoms in children from lower SES groups. This is not explained by increased parental smoking in lower SES groups as the results were controlled for smokers in the household.

TABLE 1 Observed asthma prevalence (%) by socioeconomic group

	Socioeconomic group					Total (n=1050)	p value
	1 (n=124)	2 (n=299)	3 (n=344)	4 (n=205)	5 and 6 (n=78)		
Any wheeze/exercise wheeze ever	21.8	24.7	28.8	29.3	33.3	27.2	0.029
Any wheeze/exercise wheeze in the last 12 months	11.3	14.7	19.5	14.1	20.5	16.2	0.046
Asthma diagnosed ever	12.9	14.7	14.0	14.1	16.7	14.3	0.372
BHR on testing	21.0	20.4	21.8	18.0	19.2	20.4	0.903
BHR + any wheeze/exercise wheeze ever	10.5	11.4	13.7	10.7	12.8	12.0	0.379
BHR + any wheeze/exercise wheeze in last 12 months	8.1	8.0	11.9	7.3	10.3	9.3	0.412
BHR + asthma diagnosed ever	8.1	8.4	9.9	7.3	10.3	8.8	0.387

2023379796

TABLE 2 Prevalence (%) of asthma medication by socioeconomic group in children using two definitions of asthma

	Socioeconomic group		
	1-2	3	4-6
Any wheeze/exercise in last 12 months	(n=58)	(n=67)	(n=45)
Bronchodilators	65.5	49.3	51.1
Prophylactic drugs	36.2	20.9	17.8
BHR and any wheeze/exercise wheeze in last 12 months	(n=34)	(n=41)	(n=23)
Bronchodilators	76.5	70.7	65.2
Prophylactic drugs	41.2	29.3	26.1

Some workers consider that BHR is useful for the diagnosis of asthma in epidemiological surveys as it is an objective test, most current asthmatics exhibit BHR and BHR correlates with the severity of asthma.<sup>14</sup> This study found no relationship between SES and BHR or any combination of BHR with symptoms and asthma diagnosis.

This study suggests there is no relationship between SES and asthma prevalence in children. The finding of an increased prevalence of wheeze in low SES groups might be caused by an increase in the prevalence of factors which trigger or manifest wheezy episodes in the predisposed child. Such factors include respiratory tract infections,<sup>15</sup> which have been found to be more common in low SES groups, and house dust mites, which are found in higher concentrations in damp environments which probably occur more frequently in houses of poor families.

The finding of less frequent use of asthma medications in lower SES groups with current symptoms has been described<sup>16</sup> and is consistent with described social inequities in health.<sup>1,17</sup> There are a number of possible explanations for this finding. One possibility is that prescribing by the medical practitioner may vary according to the SES group of the child and their family. Alternatively there may be no difference in prescribing patterns, but rather a difference in uptake. Finally it may be that children with lower SES families have poorer, less regular and less frequent contact with medical practitioners and thus miss the opportunity for prescription of asthma drugs.

#### ACKNOWLEDGEMENTS

Supported by the Medical Research Council of New Zealand and the Asthma Foundation of New Zealand.

#### REFERENCES

- Egbonu L, Starfield B. Child Health and Social Status. *Pediatr* 1982; 69: 550-7.
- Mitchell R G, Dawson B. Educational and social characteristics of children with asthma. *Arch Dis Child* 1973; 48: 467-71.
- Peckham C, Butler N. A national study of asthma in childhood. *Epidemiol Comm Health* 1978; 32: 79-85.
- Graham P J, Rutter M L, Yule W, Pless J B. Childhood asthma, a psychosomatic disorder? *Br J Prev Soc Med* 1967; 21: 78-85.
- Hamman R F, Hall T, Holland W W. Asthma in school children, demographic associations and peak expiratory flow rates compared in children with bronchitis. *Br J Prev Soc Med* 1975; 29: 228-38.
- McNicol K N, Williams H E, Allan J, McAndrew I. Spectrum of asthma in children—III. Psychological and social components. *Br Med J* 1973; 4: 16-20.
- Mak H, Johnston P, Abbey H, Talamo R C. Prevalence of asthma and health service utilization of asthmatic children in an inner city. *J Allergy Clin Immunol* 1982; 70: 367-72.
- Horwood L J, Fergusson D M, Shannon F T. Social and familial factors in the development of early childhood asthma. *Pediatr* 1983; 78: 859-66.
- Anderson H R, Bland J M, Patel S, Peckham C. The natural history of asthma in childhood. *J Epidemiol Comm Health* 1986; 40: 121-9.
- Asher M I, Pattemore P K, Harrison A C, Mitchell E A, Rea H H, Stewart A W, Woolcock A J. International comparison of the prevalence of asthma symptoms and bronchial hyperresponsiveness. *Am Rev Respir Dis* 1988; 138: 524-9.
- Yan K, Salome C, Woolcock A J. Rapid method for measurement of bronchial responsiveness. *Thorax* 1983; 38: 760-5.
- Johnston R. A revision of socio-economic indices for New Zealand. Wellington (NZ), New Zealand Council for Educational Research 1983.
- Speight A N, Lee D A, Hey E N. Underdiagnosis and undertreatment of asthma in childhood. *Br Med J* 1983; 286: 1253-6.
- Woolcock A J, Yan K, Salome C M, Sedgwick C J, Peat J. What determines the severity of asthma? *Chest* 1985; 87: 209s-213s.
- Minor T E, Dick E C, DeMeo A N, Ouellette J J, Cohen M, Reed C E. Viruses as precipitants of asthmatic attacks in children. *JAMA* 1974; 227: 292-8.
- Anderson H R, Bailey P A, Cooper J S, Palmer J C. Influence of morbidity, illness label, and social, family and health service factors on drug treatment of childhood asthma. *Lancet* 1981; 2: 1030-2.
- Inequalities in health: Report of a DHSS research working group. London, Department of Health and Social Security 1980.

(Revised version received April 1989)

2023379798

Pope, C.A. "Respiratory Disease Associated with Community Air Pollution and a Steel Mill, Utah Valley" AJPH 79(5): 623-628, 1989.

**ABSTRACT:** This study assessed the association between hospital admissions and fine particulate pollution ( $PM_{10}$ ) in Utah Valley during the period April 1985-February 1988. This time period included the closure and reopening of local steel mill, the primary source of  $PM_{10}$ . An association between elevated  $PM_{10}$  levels and hospital admissions for pneumonia, pleurisy, bronchitis, and asthma was observed. During months when 24-hour  $PM_{10}$  levels exceeded  $150 \mu g/m^3$ , average admissions for children nearly tripled; in adults, the increase in admissions was 44 per cent. During months with mean  $PM_{10}$  levels greater than or equal to  $50 \mu g/m^3$  average admissions for children and adults increased by 89 and 47 per cent, respectively. During the winter months when the steel mill was open,  $PM_{10}$  levels were nearly double the levels experienced during the winter months when the mill was closed. This occurred even though relatively stagnant air was experienced during the winter the mill was closed. Children's admissions were two to three times higher during the winters when the mill was open compared to when it was closed. Regression analysis also revealed that  $PM_{10}$  levels were strongly correlated with hospital admissions. They were more strongly correlated with children's admissions than with adult admissions and were more strongly correlated with admissions for bronchitis and asthma than with admissions for pneumonia and pleurisy.

2023379799

# Respiratory Disease Associated with Community Air Pollution and a Steel Mill, Utah Valley

C. ARDEN POPE III, PhD

**Abstract:** This study assessed the association between hospital admissions and fine particulate pollution ( $PM_{10}$ ) in Utah Valley during the period April 1985–February 1988. This time period included the closure and reopening of the local steel mill, the primary source of  $PM_{10}$ . An association between elevated  $PM_{10}$  levels and hospital admissions for pneumonia, pleurisy, bronchitis, and asthma was observed. During months when 24-hour  $PM_{10}$  levels exceeded  $150 \mu\text{g}/\text{m}^3$ , average admissions for children nearly tripled; in adults, the increase in admissions was 44 per cent. During months with mean  $PM_{10}$  levels greater than or equal to  $50 \mu\text{g}/\text{m}^3$  average admissions for children and adults increased by 89 and 47 per cent, respectively. During the winter months when the steel mill was open,  $PM_{10}$  levels

were nearly double the levels experienced during the winter months when the mill was closed. This occurred even though relatively stagnant air was experienced during the winter the mill was closed. Children's admissions were two to three times higher during the winters when the mill was open compared to when it was closed. Regression analysis also revealed that  $PM_{10}$  levels were strongly correlated with hospital admissions. They were more strongly correlated with children's admissions than with adult admissions and were more strongly correlated with admissions for bronchitis and asthma than with admissions for pneumonia and pleurisy. (*Am J Public Health* 1989; 79:623–628.)

## Introduction

On March 20, 1984, the US Environmental Protection Agency (EPA) proposed changes in the national ambient air quality standards for particulate pollution. Total suspended particulates (TSP) was to be replaced with a new indicator of particulate pollution that includes only those particulates with an aerodynamic diameter equal to or less than a nominal 10 micrometers ( $PM_{10}$ ). On July 1, 1987, the EPA announced its final decision. The previous primary TSP standards were to be replaced, effective July 31, 1987, with a 24-hour  $PM_{10}$  standard of 150 micrograms per cubic meter ( $\mu\text{g}/\text{m}^3$ ) with no more than one expected exceedance per year and an annual  $PM_{10}$  standard of an expected arithmetic mean of  $50 \mu\text{g}/\text{m}^3$ .<sup>1</sup>

Earlier studies of the health effects of particulate pollution<sup>2–4</sup> revealed a possible connection between air pollution and human health, and launched a wave of research exploring this connection.<sup>5–19</sup> Recent research has observed that even moderately elevated concentrations of particulate pollution may result in reductions in children's pulmonary function<sup>20,21</sup> and increased risk for bronchitis and other respiratory illnesses.<sup>22</sup> Other recent research questions the existence of a threshold level.<sup>1,23</sup>

Previous studies have not used  $PM_{10}$  as an indicator of particulate pollution. Recent experiences in Utah County have provided a unique opportunity to investigate a possible association between respiratory health and different levels of  $PM_{10}$ . Utah Valley has had daily monitoring of  $PM_{10}$  since April 1985; it has an extremely low percentage of smokers; it has experienced a prolonged shut-down and then reopening of the steel mill, its largest source of particulate pollution; over time, since monitoring of  $PM_{10}$  began, the valley has experienced considerable variability in levels of fine particulate pollution; and hospital inpatient admissions data for respiratory illnesses can be obtained. The objective of this paper is to report what has been observed in Utah Valley with respect to hospital admissions for respiratory illnesses and  $PM_{10}$  levels.

Address reprint requests to C. Arden Pope III, PhD, Associate Professor of Natural Resource and Environmental Economics, Brigham Young University, Provo, UT 84602. This paper, submitted to the *Journal* June 6, 1988, was revised and accepted for publication November 7, 1988.

© 1989 American Journal of Public Health 0090-0036/89\$1.50

## Methods

### Study Area

Utah Valley, located in Utah County of Central Utah, is the third largest county in the state with a population of 258,000 in 1987.<sup>24</sup> Approximately two-thirds of the population resides in five nearly contiguous cities situated on a valley floor with an elevation of approximately 1,402 meters above sea level bordered east and west by mountains (Figure 1).

Based on an unpublished 1986 Utah State Department of Health survey, only 5.5 per cent of Utah County's adults (18 years of age or older) smoke; approximately 90 per cent of its

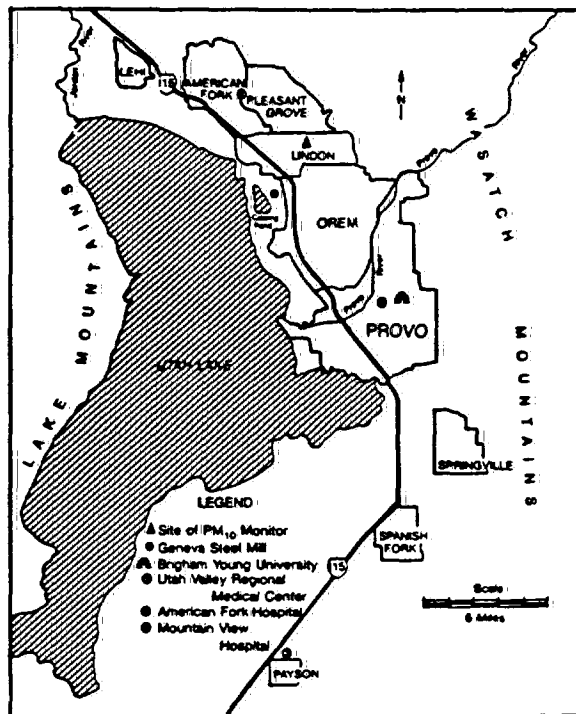


FIGURE 1—Study Area, Utah Valley.



residents are members of the Church of Jesus Christ of Latter-Day Saints (Mormon)<sup>25,26</sup> which has strong church teachings against smoking.

Monitoring of particulate pollution began in 1964 and for carbon monoxide in 1971. On March 3, 1978, the EPA designated the county as a non-attainment area in accordance with provisions of Section 107 of the Clean Air Act. EPA ambient air quality standards for TSP and carbon monoxide were often exceeded at monitoring sites at Provo, Lindon, and Pleasant Grove during winter months when temperature inversions trapped emissions in stagnant air near the valley floor.

Generally, the county experienced improvements with respect to carbon monoxide pollution in the 1980s. At one monitoring site, the number of exceedances of the maximum eight-hour primary health standard for carbon monoxide fell from a high of 52 exceedances in 1982 to 10 exceedances in 1985. In order to continue to reduce levels of carbon monoxide pollution in the county, an automobile inspection/maintenance and anti-tampering program was implemented in 1986.

Particulate pollution levels in the county remained about the same from 1979–85. The 24-hour TSP standard of  $260 \mu\text{g}/\text{m}^3$  was exceeded as many as 10–18 times per year. The average annual geometric mean from 1979–85 for TSP at the Lindon monitor equalled  $65 \mu\text{g}/\text{m}^3$ . This mean level of TSP exceeded EPA's annual secondary standard of  $60 \mu\text{g}/\text{m}^3$  but not the annual primary health standard of  $75 \mu\text{g}/\text{m}^3$ . Monitoring of sulfur dioxides ( $\text{SO}_2$ ) was conducted in the county in the 1970s but was discontinued because  $\text{SO}_2$  levels were substantially below the annual primary health standard of .03 ppm, the 24-hour primary health standard of .14 ppm and the secondary 3-hour standard of .5 ppm.

The primary industrial source of fine particulate pollution as measured by  $\text{PM}_{10}$  in Utah County is the Geneva steel mill, commonly referred to as Geneva, located near Orem (Figure 1). When in operation, the mill emits approximately 82 per cent of all industrial sources of  $\text{PM}_{10}$  including power generation.<sup>27</sup> When all sources are accounted for, Geneva's contribution to  $\text{PM}_{10}$  equals 47 to 80 per cent of total emissions.<sup>27</sup> Other sources of  $\text{PM}_{10}$  include wood burning (approximately 16 per cent), road dust (approximately 11 per cent), diesel fuel and oil combustion (approximately 7 per cent). Also, Geneva's contribution to the county's industrial emissions of sulfur oxides, nitrogen oxides, hydrocarbons, and carbon monoxides are approximately 95, 98, 86, and 82 per cent, respectively.<sup>27</sup>

Geneva was built for the US Government in the early 1940s as part of the World War II effort. It was sold to US Steel Corp in 1946. On August 1, 1986, the Geneva steel mill shut down as a result of a labor dispute with USX Corporation (previously US Steel Corp.) The plant reopened on September 1, 1987 under a new owner, Basic Manufacturing and Technologies of Utah, Inc. In April 1985, the Bureau of Air Quality began to daily monitor  $\text{PM}_{10}$  at a site in Lindon (Figure 1) using a Sierra Anderson high volume sampler. During the winter season of 1985/86, Geneva was still open and 24-hour  $\text{PM}_{10}$  levels exceeded  $150 \mu\text{g}/\text{m}^3$  on 13 occasions. The highest single day concentration was  $365 \mu\text{g}/\text{m}^3$ . During the winter of 1986/87 while Geneva was shut down, 24-hour  $\text{PM}_{10}$  levels never exceeded  $150 \mu\text{g}/\text{m}^3$ . During the winter of 1987/88, following the reopening of Geneva, 24-hour  $\text{PM}_{10}$  levels exceeded  $150 \mu\text{g}/\text{m}^3$  on 10 occasions with a single day high at 223 (Figure 2).

During the winter of 1985/86, a random sample of county residents indicated that most residents thought that air quality was a serious problem and 29 per cent indicated that they had one or more members of their family who had health problems that were aggravated by air pollution.<sup>28</sup> During the winter of

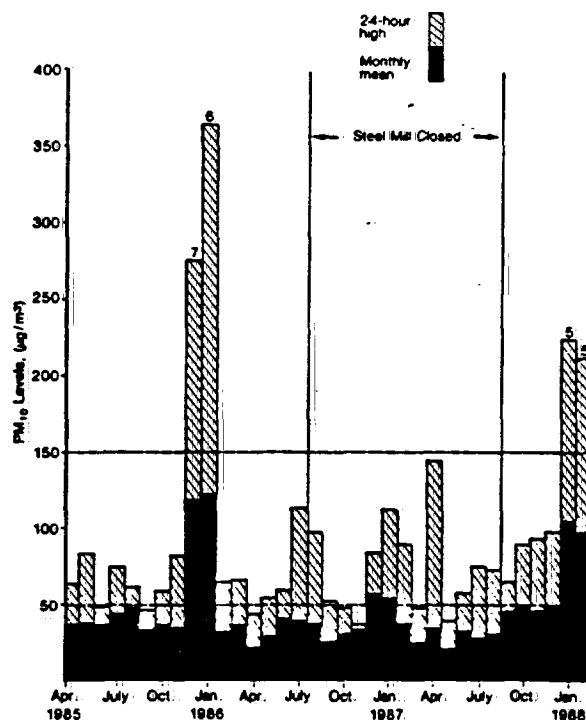


FIGURE 2—Monthly Mean and 24-Hour High  $\text{PM}_{10}$  (fine particulate pollution) Levels, Utah Valley, April 1985–January 1988

1987/88, following the closure and subsequent reopening of the steel mill, there was much local discussion about the contrast in air quality. The frequency and severity of respiratory illnesses were commonly perceived to have dropped when the mill was shut down, and then dramatically increased when it reopened. Newspaper articles, letters to the editor, and testimonials in public meetings often reflected this perception by many in the community.

#### Health Data

Hospital admissions data for respiratory-related illnesses were collected from April 1985 through February 1988. There were only four hospitals in the county. Data were collected from three of them that together had 579 beds. The other hospital in the County had only 20 beds, no pediatrics unit, no pulmonologist on its staff, and rarely provided inpatient care for respiratory illnesses.

A preliminary study of diagnosis-related groups (DRGs)<sup>29</sup> at Utah Valley Regional Medical Center indicated that DRGs 79, 80, and 81 (Respiratory Infections and Inflammations), DRGs 85 and 86 (Pleural Effusion), DRG 87 (Pulmonary Edema and Respiratory Failure), DRG 88 (Chronic Obstructive Pulmonary Disease), DRGs 92 and 93 (Interstitial Lung Disease), and DRGs 99 and 100 (Respiratory Signs and Symptoms) accounted for only 4.9, 0.6, 1.6, 3.3, 0.8, and 5.8 per cent of the collected cases, respectively. Initial comparative statistical analysis and regression analysis did not reveal any association between the closing and subsequent reopening of Geneva or  $\text{PM}_{10}$  levels and hospital admissions for any of these DRGs individually or collectively.

The bulk of the respiratory illness (83 per cent) were for the six DRGs that included 89, 90, and 91 (Simple Pneumonia and

2023379801

Pleurisy) and 96, 97, and 98 (Bronchitis and Asthma) with 42 and 41 per cent of the cases, respectively. As a result, this analysis focuses on hospital admissions where the principal diagnosis was classified within one of these six DRGs.

Monthly admissions data for these six DRGs were compiled for each of the three hospitals. Records for outpatient and emergency admissions were not complete or consistent for the full time period. Therefore, only inpatient data were used in this analysis. Accurate records for Mountain View Hospital were available for the time periods April 1985 through September 1986 and January 1987 through February 1988. Accurate inpatient records for the other two hospitals were available from April 1985–February 1988.

#### Analysis Conducted

Utah Valley Regional Medical Center's admissions were sorted into in-county and out-of-county admissions. Both Utah Valley Regional Medical Center and American Fork Hospital are located within the central urban area of the county, near the major sources of pollution. The primary analysis used the combined Utah Valley Community Hospital in-county admissions and American Fork Hospital admissions as an indicator of the level of relatively severe respiratory illness in the urban area of the county.

Three other sets of hospital admissions data were used as control variables: "all-other" admissions from Utah Valley Regional Medical Center and American Fork Hospital, excluding in-county admissions for pneumonia, pleurisy, bronchitis and asthma; out-of-county admissions to Utah Valley Regional Medical Center for pneumonia, pleurisy, bronchitis, and asthma; and admissions to Mountain View Hospital in Payson for the same illnesses.

Hospital admission levels were compared across months with different levels of particulate pollution as measured by  $PM_{10}$ . Admission levels were also compared across comparable periods of time when the steel mill was open, closed, and then reopened. Finally, monthly hospital emissions were regressed on  $PM_{10}$  levels and weather variables obtained at Brigham Young University.<sup>30</sup>

#### Results

##### Comparative Analysis

As can be seen in Figure 2, there was considerable variability in  $PM_{10}$  levels in the county over the study period.

During those months when exceedances of the 24-hour  $PM_{10}$  standard of  $150 \mu\text{g}/\text{m}^3$  occurred, the number of admissions for children, 0–17 years of age, was nearly triple the number of admissions for months with no exceedances (Table 1). In adults, admissions were approximately 44 per cent higher during the months when exceedances occurred.

During months when the arithmetic mean  $PM_{10}$  levels were equal to or greater than  $50 \mu\text{g}/\text{m}^3$ , children admissions were nearly double than when the average  $PM_{10}$  levels were less than  $50 \mu\text{g}/\text{m}^3$ . Adult admissions were increased by approximately 47 per cent.

The above comparisons were complicated by the fact that the months with especially high levels of particulate pollution were during the winter, and the reason for the high incidence of respiratory illness may be at least partly attributed to winter weather. The intermittent operation of the steel mill provided the opportunity to compare different winter seasons with marked differences in  $PM_{10}$  levels. Figure 2 demonstrates that when the steel mill was closed,  $PM_{10}$  levels were relatively low. One concern about making observations pertaining to these time periods is that the winter when the Geneva steel mill was closed may have had relatively good weather conditions and limited conditions of stagnant air. Weather data indicated that temperatures fell below zero on only two occasions throughout the study period, both in January of 1988 when they fell as low as  $-1^\circ$  and  $-7^\circ$ . Snowfall during this time period for 1985/86, 1986/87, and 1987/88 totaled only 45.5, 33.5 and 27.5 inches, respectively.<sup>30</sup>

The National Weather Service computes an air stagnation or clearing index for valleys in Western Utah, including Utah Valley.<sup>31</sup> The index ranges from 0–1000 with lower values indicating more stagnant air. When the index is less than 200 pollution dispersal is "very poor" and weather conditions are such that air pollution potential is high. The month with the lowest average clearing index occurred during the winter the mill was closed. The average clearing index for the winter period of December–February for 1985/86, 1986/87, and 1987/88 was 388, 345, and 367, respectively, and the number of days when the index was below 200 for the same time periods equalled 47, 54, and 47, respectively.<sup>32</sup> Based on this index the air was relatively more stagnant and had higher air pollution potential during the winter when the mill was shut down than the previous or following winters.

Table 2 presents comparisons of hospital admissions be-

TABLE 1—Comparisons of Monthly Average Number of Hospital Inpatient Admissions for Utah Valley Regional Medical Center and American Fork Hospital across Months with Different Levels of  $PM_{10}$ <sup>a</sup>

Months Included	Number of Months Included	Mean $PM_{10}$ Level for Months Included	Mean High $PM_{10}$ Level for Months Included	Bronchitis and Asthma Ages 0–17	Bronchitis and Asthma Age 18+	Simple Pneumonia and Pleurisy Age 0–17	Simple Pneumonia and Pleurisy Age 18+	Subtotal Ages 0–17 <sup>b</sup>	Subtotal Age 18+ <sup>b</sup>	TOTAL <sup>b</sup>
All months	35	45.8 (4.3)	94.7 (11.9)	12.5 (1.6)	17.5 (1.0)	12.0 (1.5)	22.7 (1.6)	24.5 (2.8)	40.2 (2.3)	64.7 (4.5)
Months when 24-hour $PM_{10} < 150 \mu\text{g}/\text{m}^3$	31	37.5 (1.6)	72.3 (4.4)	10.5 (1.2)	16.9 (1.0)	9.9 (1.1)	21.4 (1.3)	20.4 (1.9)	38.3 (2.0)	58.6 (3.5)
Months when 24-hour $PM_{10} \geq 150 \mu\text{g}/\text{m}^3$	4	110.3 (5.5)	268.5 (35.0)	27.8 (6.7)	22.3 (2.9)	28.3 (4.6)	33.0 (8.1)	56.0 (11.1)	55.3 (10.0)	111.3 (14.0)
Months when mean $PM_{10} < 50 \mu\text{g}/\text{m}^3$	27	35.1 (1.3)	68.7 (4.6)	10.1 (1.3)	16.5 (1.1)	10.2 (1.2)	19.8 (1.2)	20.3 (2.1)	36.3 (2.0)	56.7 (3.9)
Months when mean $PM_{10} \geq 50 \mu\text{g}/\text{m}^3$	8	82.0 (11.0)	182.5 (36.4)	20.4 (4.4)	20.8 (1.8)	18.0 (4.5)	32.5 (3.9)	38.4 (8.5)	53.3 (5.1)	91.6 (10.0)

<sup>a</sup>Standard errors at the means are presented in parentheses.

<sup>b</sup>Total may not sum up exactly due to rounding error.

tween fall and winter periods when the steel mill was open, closed, and reopened. During the winter months from December to February, hospital admissions for children were approximately three times as high when the steel mill was open than when it was closed. Even during the Fall months (September–November) when no exceedances for the 24-hour primary health standard occurred, children admissions for bronchitis and asthma were approximately twice as high when the steel mill was open. Adult hospital admissions were not as obviously associated with the reductions of  $PM_{10}$  that accompanied the closure of the steel mill. There was, however, a notable increase in adult admissions following the reopening of the mill.

#### Regression Analysis

The results of some of the regression models are presented in Table 3. Model 1 regresses total monthly hospital admissions for pneumonia, pleurisy, bronchitis, and asthma on current and lagged  $PM_{10}$  levels. All lagged variables simply refer to the previous month's value. The results demonstrate a strong correlation between admissions and  $PM_{10}$ . In fact, 59 per cent of the variance in monthly admissions for these respiratory illnesses is explained by current and lagged monthly mean  $PM_{10}$  levels alone.

In Model 2, current and lagged mean low temperature variables were also included. This relatively simple linear model with only  $PM_{10}$  and temperature variables explains 83 per cent of the variance in total hospital admissions for these respiratory illnesses. The correlation between mean  $PM_{10}$  levels, mean low temperatures and hospital admissions is particularly striking when actual admissions and estimated admissions based on Model 2 are plotted together over time (Figure 3). Models 3–14 repeat the analysis done in Models 1 and 2 for total adult admissions, total children admissions, adult admissions for pneumonia and pleurisy, children admissions for pneumonia and pleurisy, adult admissions for bronchitis and asthma, and children admissions for bronchitis and asthma.

Autocorrelated errors exist with some of the models, particularly those with only  $PM_{10}$  levels as independent variables. This autocorrelation, however, is largely eliminated when weather variables are included. For example, the Durbin-Watson D statistic is 1.0 for Model 1 and 1.6 for Model 2. It is 1.3 for Model 3 and 2.0 for Model 4. There is also collinearity between  $PM_{10}$  levels and temperature. The correlation coefficient between the mean low temperature and monthly mean  $PM_{10}$  levels equals  $-0.32$ . This collinear-

ity complicates the analysis and makes specific best point estimators of the correlation coefficients difficult to estimate. However, Model 2 was reestimated using a nonlinear quasi-Newton iterative procedure which gave identical regression coefficients with somewhat smaller standard-errors.

Numerous other regression models were estimated that included snowfall, rainfall, evaporation, monthly mean temperatures, and mean high temperatures. The weather variable that was consistently most highly correlated with admissions was the mean low temperature. Regressions that used  $PM_{10}$  levels lagged for two months, and dummy variables that indicated the opening and closing of the steel mill and inversion seasons were also tried. Even with the inclusion of these other variables, strong, positive, correlations between hospital admissions and  $PM_{10}$  levels remained. Regression models were also estimated with monthly 24-hour high  $PM_{10}$  levels used as independent variables. The results were similar to those in Models 1–14 as presented in Table 3, but 24-hour high  $PM_{10}$  levels were generally not as strongly correlated with admissions as were the mean  $PM_{10}$  values.\*

#### Analysis with Control Variables

Neither comparative analysis nor regression analysis revealed any associations between the control variables and  $PM_{10}$  levels or the closing and reopening of the steel mill. "All-other" admissions that excluded in-county admissions for pneumonia, pleurisy, bronchitis, and asthma averaged 1,562 per month and appeared to be declining slightly over the study period. No seasonal variability nor any association with  $PM_{10}$  levels or the closing and reopening of the mill was observed. Monthly "all-other" admissions regressed on  $PM_{10}$  levels and temperature variables (Models 15 and 16 in Table 3) showed no significant correlation with  $PM_{10}$  levels.

Out-of-county hospital admissions to Utah Valley Regional Medical Center and admissions to Mountain View Hospital in Payson were regressed on  $PM_{10}$  levels and temperature variables. Models 17 and 18 in Table 3 present the results of the regressions for total out-of-county admissions for pneumonia, pleurisy, bronchitis, and asthma. The same regressions were also run on out-of-county and Mountain View Hospital with admissions broken down by adults, children, and respiratory illnesses, as done in Models 1–14.

\*Data available upon request to author.

TABLE 2—Comparisons of Hospital Inpatient Admissions for Utah Valley Regional Medical Center and American Fork Hospital across Time Periods with Geneva Steel Mill Open and Closed

Year	Steel Mill Open?	Mean $PM_{10}$ Level for Months Included	Mean High $PM_{10}$ Level for Months Included	Bronchitis and Asthma Ages 0–17	Bronchitis and Asthma Age 18+	Simple Pneumonia and Pleurisy Ages 0–17	Simple Pneumonia and Pleurisy Age 18+	Subtotal Ages 0–17	Subtotal Age 18+	TOTAL
Winter Months (December–February)										
1985/86	yes	90	235	78	75	76	73	154	148	302
1986/87	no	51	96	23	67	32	83	55	150	205
1987/88	yes	64	177	78	65	71	126	149	191	340
Fall Months (September–November)										
1985	yes	35	63	49	46	20	51	69	97	166
1986	no	31	47	23	48	25	60	48	108	156
1987	yes	47	83	55	46	24	66	79	112	191
Fall and Winter (September–February)										
1985/86	yes	63	149	127	121	96	124	223	245	468
1986/87	no	41	71	46	115	57	143	103	258	361
1987/88	yes	66	130	133	111	95	192	228	303	531

## RESPIRATORY DISEASE AND COMMUNITY AIR POLLUTION

TABLE 3—Sample Results of Multiple Regression Analysis

Model	Dependent Variable:	Regression Coefficients <sup>a</sup>					R <sup>2</sup>
		Constant	PM <sub>10</sub> Mean	Lagged PM <sub>10</sub> Mean	Low Temperature	Lagged Low Temperature	
1	Total	21.18 (7.1)	0.357 (.14)	0.599 (.15)	—	—	.59
2	Total	95.54 (12.8)	0.119 (.11)	0.339 (.11)	-0.351 (.30)	-0.929 (.31)	.83
3	Total Adult	25.31 (4.8)	0.150 (.09)	0.175 (.10)	—	—	.26
4	Total Adult	73.65 (9.4)	-0.016 (.08)	0.017 (.08)	-0.347 (.22)	-0.486 (.23)	.64
5	Total Child	-4.14 (4.0)	0.207 (.08)	0.425 (.08)	—	—	.67
6	Total Child	21.89 (9.7)	0.135 (.06)	0.321 (.06)	-0.004 (.23)	-0.443 (.24)	.75
7	Pn/Pl Adult	14.57 (3.5)	0.139 (.07)	0.034 (.07)	—	—	.19
8	Pn/Pl Adult	46.84 (7.3)	0.020 (.06)	-0.063 (.06)	-0.305 (.17)	-0.252 (.18)	.54
9	Pn/Pl Child	-1.50 (2.5)	0.112 (.05)	0.183 (.05)	—	—	.53
10	Pn/Pl Child	15.49 (5.3)	0.086 (.04)	0.095 (.05)	0.196 (.13)	-0.487 (.13)	.72
11	Br/As Adult	10.74 (2.0)	0.011 (.04)	0.140 (.04)	—	—	.36
12	Br/As Adult	26.81 (4.3)	-0.037 (.04)	0.081 (.04)	-0.042 (.10)	-0.234 (.11)	.59
13	Br/As Child	-2.63 (2.5)	0.094 (.05)	-0.241 (.05)	—	—	.60
14	Br/As Child	6.40 (6.5)	0.049 (.05)	0.226 (.06)	-0.201 (.15)	0.044 (.16)	.64
15	All-Other	1586 (46)	-0.050 (.9)	-0.604 (1.0)	—	—	.02
16	All-Other	1482 (120)	0.840 (1.0)	-0.798 (1.0)	5.904 (2.8)	-4.069 (2.9)	.15
17	Out-of-County Total	15.09 (2.9)	-0.047 (.02)	-0.006 (.03)	0.123 (.07)	-0.264 (.07)	.43
18	Mountain View Total	33.38 (6.8)	-0.013 (.05)	-0.041 (.06)	0.073 (.16)	-0.474 (.16)	.46

<sup>a</sup>The absolute value of the standard errors is provided in parentheses.

Pn/Pl=pneumonia/pleurisy

Br/As=bronchitis/asthma

Although Payson is located in the county and should be similarly influenced by contagious illness, it is over 32 kilometers from the major sources of pollution and should not be as influenced by monitored levels of PM<sub>10</sub>.

The regressions using out-of-county and Mountain View Hospital admissions are limited by the fact that only about 15 per cent of Utah Valley Regional Medical Center admissions are out-of-county, and Mountain View Hospital's data are missing for the months of October, November, and December of 1986. The results indicated that there was significant correlation between the mean low temperature lagged variable similar to those in the earlier regressions. There was no positive correlation between out-of-county or Mountain View Hospital admissions and PM<sub>10</sub> levels, however.

### Discussion

The results indicated that hospital admissions for respiratory illnesses were strongly associated with PM<sub>10</sub> levels. This association is much stronger for children than adults, and somewhat stronger for bronchitis and asthma than for pneumonia and pleurisy. These associations were particularly strong with monthly lagged variables suggesting that the health effects of particulate pollution are cumulative and that it takes time before they are manifested in inpatient hospital admissions data.

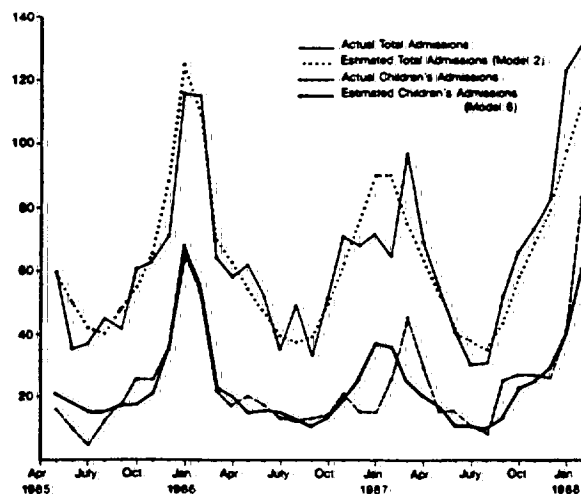


FIGURE 3—Actual and Estimated Hospital Admissions, April 1985 through January 1988, Utah Valley

Also, increased admissions for children are observed even for months when  $PM_{10}$  did not exceed  $150 \mu g/m^3$ , suggesting that this standard may not be adequate protection for some children.

There are several concerns about these observations. One concern is that if increases in contagious illnesses such as influenza by chance coincided with periods of high  $PM_{10}$  levels, particularly during the winters when the steel mill was open, then the observed correlation between  $PM_{10}$  and admissions may be spurious. It would be expected, however, that if this were the case, the same correlation would be found in hospital admissions from neighboring counties or communities unaffected by Utah Valley's principal sources of pollution. No such correlation was found for out-of-county admissions to Utah Valley Regional Medical Center or to Mountain View Hospital in nearby Payson. Nor was such correlation found between  $PM_{10}$  levels and non-respiratory hospital admissions.

Another concern is that often levels of several air pollutants rise and fall in concert.  $PM_{10}$  may be a surrogate for other air pollutants with which it is temporarily associated. Two pollutants that may have had similar impacts on respiratory illnesses during the study period are total suspended particulates and ozone. Because  $PM_{10}$  measures only relatively small particles of particulate pollution, and because it is the smaller particles that are expected to pose the greatest health risks, it is considered the most appropriate measure of particulate pollution as it relates to respiratory health.<sup>1</sup> Regression models estimated with monthly mean total suspended particulate levels used as independent variables yielded results similar to Models 1-14 presented in Table 3 which used  $PM_{10}$ . The correlations between admissions and total suspended particulates were generally not as strong as those between admissions and  $PM_{10}$ .

There was no evidence that suggested that  $PM_{10}$  was serving as a surrogate for ozone pollution. The only times ozone pollution in Utah Valley rose to levels of any consequence was in the summer months during hot sunny days, whereas the periods of high levels of  $PM_{10}$  and hospital admissions for respiratory illness occurred mostly during the winter months when the steel mill was in operation. The results of this study suggest that the dominant pollution in terms of its impact on respiratory health in Utah Valley is particulate pollution and that  $PM_{10}$  is a better indicator than TSP.

Finally, the association between respiratory illness and particulate pollution found in this study is relatively large as compared with some previous studies.<sup>20-22,33</sup> This relatively strong association can be explained in part because  $PM_{10}$  is a better indicator of particulate pollution as it relates to respiratory health than previously used indicators.<sup>1</sup> Also, because Utah Valley experiences relatively high levels of particulate pollution, yet has an extremely low portion of its population that smoke, particulate pollution is likely a relatively large contributor to respiratory disease in the county.

#### ACKNOWLEDGMENTS

Special thanks are given to Victor Archer, MD, Clark Bishop, MD, Don Bloxham, PhD, Joseph Miner, MD, and Henry Yeates, MD, as well as personnel at the Utah Bureau of Air Quality; Utah Valley Regional Medical Center; American Fork Hospital; and Mountain View Hospital for providing information, data, helpful suggestions, and reviews of earlier drafts of this manuscript.

#### REFERENCES

- US Environmental Protection Agency: Revisions to the National Ambient Air Quality Standards for Particulate Matter. Federal Register July 1, 1987; 52:(126)24634-24669.
- Ciocco A, Thompson DJ: A follow-up on Donora ten years after: methodology and findings. *Am J Public Health* 1961; 51:155-164.
- Firket J: The cause of the symptoms found in the Meuse Valley during the fog of December, 1930. *Bull Acad Roy Med Belg* 1931; 11:683-741.
- Gore AT, Shaddick CW: Atmospheric pollution and mortality in the County of London. *Br J Prev Soc Med* 1968; 12:104-113.
- Logan WPD: Mortality in London fog incident. *Lancet* 1953; 1:336-338.
- Schrenk JJ, Heimann H, Clayton GD, Gafaer W, Wexler H: Air Pollution in Donora, Pennsylvania. Epidemiology of the Smog Episode of October 1948. Public Health Bull 306. Washington DC: Govt Printing Office, 1949.
- Scott JA: The London fog of December 1962. *Med Off* 1963; 109:250.
- Waller RE, Commins BT: Episodes of high pollution in London, 1952-1966. In: Proceedings, International Clean Air Conference, Part II. London: National Society for Clean Air, 1966; 288.
- American Thoracic Society: Health Effects of Air Pollution. New York: American Lung Association, 1978.
- Cannon JS: The Health Costs of Air Pollution. New York: American Lung Association, 1985.
- Durham WH: Air pollution and student health. *Arch Environ Health* 1974; 28:241-254.
- Hammer DI, Miller FJ, Stead AG, Hayes CG: Air pollution and childhood lower respiratory disease. I. Exposure to particulate matter in New York, 1972. In: Finkel AJ, Dull WC (eds): Clinical Implications of Air Pollution Research. Acton, MA: Publishing Sciences Group, 1976.
- Holland WW, Bennett AE, Cameron IR, Du V, Florey C, Leeder SR, Schilling RSF, Swan AV, Walter RE: Health effects of particulate pollution: Reappraising the evidence. *Am J Epidemiol* 1979; 110:527-659.
- Lave LB, Seskin EP: Air Pollution and Human Health. Baltimore: John Hopkins University Press, 1977.
- Lawther PJ, Waller PE, Henderson M: Air pollution and exacerbations of bronchitis. *Thorax* 1970; 25:525-539.
- Levy D, Gent M, Newhouse MT: Relationship between acute respiratory illness and air pollution in an industrial city. *Am Rev Respir Dis* 1973; 116:167-173.
- Thibodeau LA, Reed RB, Bishop YMM, Kammerman LA: Air pollution and human health: A review and reanalysis. *Environ Health Perspect* 1980; 34:165-183.
- Ware J, Thibodeau LA, Speizer FE, Colome S, Ferris BG Jr: Assessment of the health effects of atmospheric sulfur oxides and particulate matter: evidence from observational studies. *Environ Health Perspect* 1981; 41:255-276.
- Whittenmore AS, Korn EL: Asthma and air pollution in the Los Angeles area. *Am J Public Health* 1980; 70:687-696.
- Dassen W, Brunekreef B, Hoek G, Hofschreuder P, Staatsen B, de Groot H, Schouten E, Biersteker K: Decline in children's pulmonary function during an air pollution episode. *J Air Pollut Control Assoc* 1986; 36:1223-1227.
- Dockery DW, Ware JH, Ferris BG Jr, Spierzer FE, Cook NR, Herman SM: Change in pulmonary function in children associated with air pollution episodes. *J Air Pollut Control Assoc* 1982; 32:937-942.
- Ware JH, Ferris BG Jr, Dockery DW, Spengler JD, Stram DO, Speizer FE: Effects of ambient sulfur oxides and suspended particulates on respiratory health of preadolescent children. *Am Rev Respir Dis* 1986; 133:834-842.
- Ostro BD: A search for a threshold in the relationship of air pollution to mortality: a reanalysis of data on London winters. *Environ Health Perspect* 1984; 58:397-399.
- Woods and Poole Economics, Inc: 1987 Nevada and Utah State Profile. Washington DC: Woods and Poole, Inc, 1987.
- Deseret News: 1985 Church Almanac. Salt Lake City, Utah: Deseret News; 1984.
- Johnson DW, Picard PR, Quin B: Churches and Church Membership in the United States, 1971: An Enumeration by Region, State, and County. Washington DC: Glenmary Research Center, 1974.
- Utah Bureau of Air Quality: Utah Air Emission Inventory. Salt Lake City, Utah: Utah State Department of Health, various issues 1985-87.
- Pope CA III, Miner FD Jr: Valuation of improved air quality in Utah County. *Environ Manag* 1988; 12:381-389.
- Lorenz EW, Jones MK: The Physician's DRG Working Guidebook. Washington DC: St Anthony Hospital Publications, 1987.
- Brigham Young University, Department of Geography: Weather Station Reports. Provo, Utah: Brigham Young University, 1985-88.
- Jackman DN, Chapman WT: Some meteorological aspects of air pollution in Utah with emphasis on the Salt Lake Valley. Technical Memorandum NWS WR-120. Salt Lake City, Utah: National Oceanic and Atmospheric Administration, National Weather Service, Western Region, 1977.
- National Oceanic and Atmospheric Administration, National Weather Service: Air Stagnation Index for Basin I, Western Utah. Salt Lake City, Utah: National Weather Service Western Region, April 1985-February 1988.
- Samet JM, Bishop Y, Speizer FE, Spengler JF, Benjamin GF Jr: The relationship between air pollution and emergency room visits in an industrial community. *J Air Pollut Control Assoc* 1981; 31:236-240.

2023379806



# IAQ89

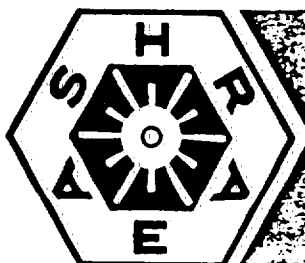
**Indoor Air Quality**  
**April 17-20, 1989**  
**San Diego, CA**

## **The Human Equation: Health and Comfort**

*Organized by the*  
**American Society of Heating,  
Refrigerating and Air-Conditioning  
Engineers, Inc.**  
*and the*  
**Society for Occupational and Environmental Health**

**IAQ89 Manufacturers' Product and Service Session**

2023379807



# IAQ 89 THE HUMAN EQUATION: HEALTH AND COMFORT

## Welcome to IAQ '89

This year's conference has been organized by:

The American Society of Heating, Refrigerating and  
Air-Conditioning Engineers, Inc.  
and

The Society for Occupational and Environmental Health.

IAQ '89 is a follow up symposium to IAQ 86, 87 and 88, and  
will present demonstrated, documented solutions to indoor air  
quality problems.

## IAQ '89 Steering Committee

**H. E. "Barney" Burroughs, Chairman**  
Consultancy of IAQ & Building Wellness  
Atlanta, GA

**David T. Grimsrud, Ph.D.**  
University of Minnesota  
Minneapolis, MN

**Philip R. Morey, Ph.D.**  
Clayton Environmental Consultants  
Wayne, PA

**Dean Baker, M.D.**  
Mt. Sinai School of Medicine  
New York, NY

**Michael J. Hodgson, M.D.**  
University of Pittsburgh  
Pittsburgh, PA

**Jonathan Samet, M.D.**  
University of New Mexico Cancer Center  
Albuquerque, NM

**Larry G. Berglund, Ph.D.**  
John B. Pierce Foundation  
New Haven, CT

**Kathleen Kreiss, M.D.**  
National Jewish Center  
Denver, CO

**John M. Talbott**  
U.S. Department of Energy  
Washington, DC

**Emerson L. Besch, Ph.D.**  
University of Florida  
Gainesville, FL

**James A Merchant, M.D.**  
Inst. of Agricultural Medicine  
and Occupational Health  
Iowa City, IA

**W. Gene Tucker, Ph.D.**  
U.S. Environmental Protection Agency  
Research Triangle Park, NC

**Harriett Burge, Ph.D.**  
University of Michigan  
Ann Arbor, MI

**Douglas S. Walkinshaw, Ph.D.**  
National Research Council  
Ottawa, Ontario, Canada

## Financial Contributors:

U.S. Department of Energy  
U.S. Environmental Protection Agency  
National Institute for Occupational Safety and Health  
National Heart, Lung and Blood Institute  
National Institute of Environmental Health Sciences

## UPCOMING ASHRAE MEETINGS

Winter	Date	Annual
	1989	Vancouver, BC June 24-28
Atlanta, GA Feb 10-14	1990	St. Louis, MO June 9-13
New York, NY Jan 19-23	1991	Indianapolis, IN June 22-26
Anaheim, CA Jan 25-29	1992	Baltimore, MD June 27-July 1

2023379808



## ASHRAE/SOEH IAQ'89 PROGRAM

**MONDAY, APRIL 17**

8:30 a.m. to 8:45 a.m.

### OPENING REMARKS

*Aviary Ballroom*

H.E. "Barney" Burroughs, *IAQ'89 Chairman*  
David S. Butler, *ASHRAE President-Elect*  
James A. Merchant, M.D., *SOEH Past President*

8:45 a.m. to 10:45 a.m.

### PANEL DISCUSSION:

#### GOVERNMENT ACTIVITIES IN INDOOR AIR QUALITY

*Aviary Ballroom*

James A. Merchant, M.D., *Panel Chairman*

### PANELISTS:

Sandra Eberle, *US Consumer Products Safety Commission*  
Richard W. Gorman, *National Institute for Occupational  
Safety and Health*  
James E. Hill, Ph.D., *National Institute of Standards and  
Technology* John Talbot  
George S. Malindzak, Ph.D., *National Institute of En-  
vironmental Health Services*  
David H. Mudarri, Ph.D., *US Environmental Protection  
Agency*  
Susan L. Rose, Ph.D., *US Department of Energy*

10:45 a.m. to 11:00 a.m. **BREAK**  
*Foyer*

11:00 a.m. to 12:30 p.m.

### TECHNICAL SESSION:

#### POLLUTANTS/HEALTH EFFECTS

*Aviary Ballroom*

Dean Baker, M.D., *Session Chairman*

#### Sick Building Syndrome Traced to Excessive Total Suspended Particulates (TSP):

C. W. Armstrong, M.D., F.A.C.P.  
P. C. Sherertz, Ph.D.  
G. C. Llewellyn, Ph.D., *Virginia Department of Health, Rich-  
mond, Virginia*

An epidemiologic and environmental investigation into the air quality of a high-rise, public office building was conducted in July, 1988. A walk-through inspection revealed particulate (dust) soiling of ceiling and work surfaces, in occupied sections of the service floor. Building air samples obtained by high-volume air pumps and cassette filters revealed elevated concentrations of total suspended particulates (TSP) which ranged up to 1.07 mg/m<sup>3</sup> (over 17 times the Building Officials and Code Administrators (BOCA) standard). In 17 (59%) of the 29 areas tested, TSP levels exceeded the BOCA standard of  $\leq 0.06$  mg/m<sup>3</sup> (annual average). Recorded temperatures, relative humidity readings, and supply of outside air were within acceptable limits. Testing for volatile organic compounds, combustion products, formaldehyde, ozone, and fungal spores revealed no levels of concern. A survey of occupants in selected units was conducted with 94% participation. Fifty-five percent indicated that they had experienced symptoms that appeared or worsened during their working hours. Of these, 47% indicated that they had missed work because of their symp-

oms. Common symptoms were headache and sinus/upper respiratory congestion, compatible with air contamination by TSP or other irritants. In multivariate analysis, illness was found to be significantly associated with air TSP concentration ( $p < 0.002$ ), CO<sub>2</sub> concentration, average number of hours worked per week, gender, and smoking status. This is one of very few outbreaks of building-related illness where occupant illness has been associated with exposure to elevated levels of an environmental contaminant (TSP).

#### Symptoms and the Micro-Environment in the Sick-Building Syndrome: A Cross-Sectional Investigation:

LMJ. Hodgson, M.D., M.P.H., *University of Pittsburgh School  
of Medicine, Pittsburgh, PA*  
P. Collopy, M.E., C.I.H., *Carnegie Mellon University,  
Pittsburgh, PA*

In a cross-sectional investigation in one building, complaints associated with the "sick building syndrome" were measured on a linear analogue scale questionnaire. At the same time, the micro-environment was characterized in the breathing zone by measuring temperature, relative humidity, respirable suspended particulates. Regression models suggested that heat load may have contributed to the level of complaints.

#### Health Effects of Heating With Wood: Chest Illness in Young Children and Indoor Heating With Woodburning Stoves:

J. S. Osborne, III, Ph.D., M.P.H., *Southwestern Michigan Area  
Health Education Center, Kalamazoo, Michigan*  
R. E. Honick, M.D., *Michigan State University College of  
Human Medicine, East Lansing, Michigan*

This study investigated a suspected relationship between the occurrence of chest illness in young children and use of woodburning stoves (WBS) for indoor heating. Data were prospectively collected during the winters of 1980, 1981, and 1982 for 62 mid-Michigan children age one to seven years (31 randomly selected children from WBS-heated homes and 31 controls from homes heated by conventional sources matched for age, sex, and place of residence). The specific a priori research hypothesis were that the proportion of children having a chest illness would be significantly greater in the WBS-group than in the control group, that a greater proportion of WBS-group children would have chest illnesses lasting at least one week, and that a greater proportion of WBS-group children would be hospitalized before age two years for chest illness.

Results showed a significant difference ( $p < 0.05$ ) between the WBS and control groups in the proportion of children having a chest illness from 1980-82 (especially bronchitis, upper respiratory infection, and pneumonia); 39% of the WBS-group and 19% of controls had at least one such illness. Further, the WBS-group had a greater proportion of chest illnesses lasting at least one week (32% vs. 16%) and a greater proportion of hospitalizations for chest illness before age two years (16% vs. 10%). These differences were not accounted for by medical histories, frequency of physician visits, sociodemographic factors, or exposure to other sources of indoor air pollution investigated in the study (i.e., parental smoking, cooking with gas, urea-formaldehyde foam insulation) and suggest that indoor heating with WBS may be a significant risk factor for chest illness in young children.

#### The Effects of Environmental Tobacco Smoke on Acute Respiratory Disease:

B. D. Ostro, Ph.D., *California Public Health Foundation,  
Berkeley, California*

There are few sources of data that provide individual-level estimates of smoking status, as well as information on exposure



Platt, S.D., Martin, C.J., Hunt, S.M., Lewis, C.W. "Damp housing, mould growth, and symptomatic health state" BMJ 298: 1673-1678, 1989.

**ABSTRACT.** Objective-To examine the relation between damp and mould growth and symptomatic ill health.

Design-Cross-sectional study of random sample of households containing children; separate and independent assessments of housing conditions (by surveyor) and health (structured interview by trained researcher).

Setting-Subjects' homes (in selected areas of public housing in Glasgow, Edinburgh, and London).

Subjects-Adult respondents (94% women) and 1169 children living in 597 households.

End points-Specific health symptoms and general evaluation of health among respondents and children over two weeks before interview; and score on general health questionnaire (only respondents).

Measurements and main results-Damp was found in 184 (30.8%) dwellings and actual mould growth in 274 (45.9%). Adult respondents living in damp and mouldy dwellings were likely to report more symptoms overall, including nausea and vomiting, blocked nose, breathlessness, backache, fainting, and bad nerves, than respondents in dry dwellings. Children living in damp and mouldy dwellings had a greater prevalence of respiratory symptoms (wheeze, sore throat, runny nose) and headaches and fever compared with those living in dry dwellings. The mean number of symptoms was higher in damp and mouldy houses and positively associated with increasing severity of dampness and mould (dose response relation). All these differences persisted after controlling for possible confounding factors such as household income, cigarette smoking, unemployment, and overcrowding. Other possible sources of bias that might invalidate the assumption of a causal link between housing conditions and ill health-namely, investigator bias, respondent bias, and selection bias-were also considered and ruled out.

Conclusion-Damp and mouldy living conditions have an adverse effect on symptomatic health, particularly among children.

2023379811

(500 IU) compared with 300 µg used in the Canadian work.<sup>3</sup>

Widespread administration of anti-D immunoglobulin antenatally in this regimen would not be possible at present because of limited supply from a decreasing pool of immunised donors. Immunoglobulin produced by genetic engineering, however, may be available soon, and trials are planned to study the effectiveness of even lower doses.

When studying a treatment regimen for any side effects it is important to avoid the bias created by considering only untoward consequences. Unexpected benefits are also possible, and we paid particular attention to any effects anti-D immunoglobulin may have had on the incidence of hypertensive disease such as pre-eclampsia. Some evidence suggests that previous blood transfusions may reduce the incidence,<sup>12</sup> and possibly some blood products also do so. The data collected, however, though not contradicting this hypothesis, showed no significant difference.

- 1 Anonymous. McMaster Conference on Prevention of Rh Immunisation. *Vox Sang* 1979;36:50-64.
- 2 Bowman JM. Controversies in Rh prophylaxis. Who needs Rh immune globulin and when should it be given? *Am J Obstet Gynecol* 1985;151:289-94.

- 3 Bowman JM, Upton B, Lewis M, Pollock JM. Rh immunization during pregnancy: antenatal prophylaxis. *Can Med Assoc J* 1978;118:623-7.
- 4 Tovey LAD. Haemolytic disease of the newborn—the changing scene. *Br J Obstet Gynaecol* 1986;93:960-6.
- 5 Blachman M, Zipursky A, Bartsch FR, Hermann M, Eklund J, Nevandlinna HR. Rh immunization during pregnancy. *Vox Sang* 1979;36:50-64.
- 6 Tovey LAD, Townley A, Stevenson BJ, Tavernier J. The Yorkshire antenatal anti-D immunoglobulin trial in primigravidae. *Lancet* 1983;ii:244-6.
- 7 Nusbacher J, Bove JR. Rh Immunoprophylaxis is antepartum therapy—desirable? *N Engl J Med* 1980;303:935-7.
- 8 Tovey GH. Should anti-D immunoglobulin be given antenatally? *Lancet* 1980;ii:466-8.
- 9 Adams MM, Marks JS, Kaplan JP. Cost implications of routine antenatal administration of Rh immune globulin. *Am J Obstet Gynecol* 1984;149:633-8.
- 10 Hensleigh PA. Preventing rhesus isomunization: Antepartum Rh immune globulin prophylaxis versus a sensitive test for risk identification. *Am J Obstet Gynecol* 1983;146:749-55.
- 11 Torrance GW, Zipursky A. Cost-effectiveness of antepartum prevention of Rh immunisation. *Clin Perinatol* 1984;11:267-81.
- 12 Hensleigh PA. Controversies in Rh prophylaxis. *Am J Obstet Gynecol* 1985;153:112.
- 13 Bowman JM. Controversies in Rh prophylaxis. *Am J Obstet Gynecol* 1985;153:112-3.
- 14 Tabach KMA, Lebberz TB, Crandall BF. Risks of prophylactic anti-D immunoglobulin after second-trimester amniocentesis. *Am J Obstet Gynecol* 1984;149:225-6.
- 15 Feeney JG, Tovey LAD, Scott JS. Influence of previous blood transfusion on incidence of pre-eclampsia. *Lancet* 1977;ii:874-5.
- 16 Perrault RA, Hogman CF. Low concentration red cell antibodies. III. Cold IgG anti D in pregnancy, incidence and significance. *Acta Universitatis Upsalienis* 1972;120:5.

(Accepted 10 April 1989.)

## Damp housing, mould growth, and symptomatic health state

Stephen D Platt, Claudia J Martin, Sonja M Hunt, Chris W Lewis

### Abstract

**Objective**—To examine the relation between damp and mould growth and symptomatic ill health.

**Design**—Cross-sectional study of random sample of households containing children; separate and independent assessments of housing conditions (by surveyor) and health (structured interview by trained researcher).

**Setting**—Subjects' homes (in selected areas of public housing in Glasgow, Edinburgh, and London).

**Subjects**—Adult respondents (94% women) and 1169 children living in 597 households.

**End points**—Specific health symptoms and general evaluation of health among respondents and children over two weeks before interview; and score on general health questionnaire (only respondents).

**Measurements and main results**—Damp was found in 184 (30.8%) dwellings and actual mould growth in 274 (45.9%). Adult respondents living in damp and mouldy dwellings were likely to report more symptoms overall, including nausea and vomiting, blocked nose, breathlessness, backache, fainting, and bad nerves, than respondents in dry dwellings. Children living in damp and mouldy dwellings had a greater prevalence of respiratory symptoms (wheeze, sore throat, runny nose) and headaches and fever compared with those living in dry dwellings. The mean number of symptoms was higher in damp and mouldy houses and positively associated with increasing severity of dampness and mould (dose response relation). All these differences persisted after controlling for possible confounding factors such as household income, cigarette smoking, unemployment, and overcrowding. Other possible sources of bias that might invalidate the assumption of a causal link between housing conditions and ill health—namely, investigator bias, respondent bias, and selection bias—were also considered and ruled out.

**Conclusion**—Damp and mouldy living conditions

have an adverse effect on symptomatic health, particularly among children.

### Introduction

Showing a direct relation between damp housing and ill health is by no means straightforward. Firstly, those living in the worst housing conditions are likely to be experiencing other forms of adversity, such as low income and unemployment. Secondly, personal behaviour may also play a part in the causation of ill health. An equally important methodological concern is the process of the data collection itself. If information about health and housing conditions is elicited in the same interview respondents may exaggerate the prevalence of problems, leading to a spurious association between the two phenomena. Moreover, the researchers themselves may influence reporting.

In 1986 we carried out a preliminary study in Edinburgh, which attempted to overcome these methodological difficulties by using a double blind research design.<sup>1</sup> Children living in damp houses, particularly where there was also mould growth, were reported to have higher rates of respiratory and gastrointestinal symptoms, aches and pains, and fever than children in dry dwellings. These differences could not be attributed to smoking or differences between damp and dry households regarding unemployment, income, overcrowding, or duration of tenancy. The numbers of households that included a child was not large enough ( $n=101$ ), however, to permit a full analysis of the role of other possible confounding variables. Accordingly, we carried out a larger scale, more detailed investigation.

### Subjects and methods

The study was conducted in three major cities: Edinburgh, Glasgow, and London. Within each city discrete geographical areas of public housing were

Medical Research Council  
Unit for Epidemiological  
Studies in Psychiatry,  
Royal Edinburgh Hospital,  
Edinburgh EH10 5HF  
Stephen D Platt, PHD,  
research sociologist

Research Unit in Health  
and Behavioural Change,  
University of Edinburgh,  
Edinburgh EH1 2QZ  
Claudia J Martin, PHD,  
research fellow  
Sonja M Hunt, PHD, senior  
research fellow

Division of Applied  
Microbiology, Department  
of Bioscience and  
Biotechnology, University  
of Strathclyde, Glasgow  
G1 1XQ  
Chris W Lewis, PHD, research  
fellow

Correspondence to: Dr  
Platt.

*Br Med J* 1989;298:1673-8

identified in which (a) families with young children predominated; (b) the prevalence of damp housing was thought to be in the range of 25-50% of total dwellings; (c) socioeconomic state was likely to be fairly homogeneous; and (d) types of housing and structures of buildings, including any renovations, could be clearly specified. Two sites were chosen in Edinburgh, two in Glasgow, and one in London. Tenants' groups were contacted and their cooperation elicited. Lists of addresses at the chosen sites were obtained from the relevant housing departments. The intention was to achieve a sample of 500 eligible households in Edinburgh and in Glasgow and 200 in London. A random sample of addresses was drawn according to the total number of dwellings in the area.

Only those households with at least one child aged under 16 were eligible for inclusion in the study. As official statistics on the exact location of families with young children were not available the sample was identified in two ways: (a) at the time of the main health interview (see below) the interviewers identified suitable families by contacting each dwelling on the list; and (b) in two of the sites members of the tenants' association identified addresses on the list containing families who met the study criteria.

Two surveyors carried out an assessment of dampness (severity and type) and mould (severity and location) and details of the structure of the dwelling. Using an air sampler (Surface Air Systems) they extracted air samples from rooms and, where visible mould growth was present, a sample from each affected room was collected. A microbiologist estimated spore counts from the air samples and identified the fungi from air and walls when possible.

We devised and pretested two survey forms. The form for the house conditions survey contained items on type of building, location, number of rooms, dampness, mould, ventilation, insulation, and renovations. The health survey was a revised version of that used by Martin *et al.* In the course of a structured interview the respondent (whenever possible the female householder) answered detailed questions about her own and her children's health during the past two weeks; smoking by all adults and children; type of heating, washing, and drying facilities; presence of pets; economic activity and occupation of all adults in the household; household income; and housing conditions and facilities.

The study was carried out during February-April 1988. Once the health interview had been completed the surveyors were instructed to visit the dwelling. The petri dishes containing air and wall mould samples were taken each day to the University of Strathclyde, where they were refrigerated and cultured. Air spore counts were calculated and fungi identified when possible. The surveyors and the microbiologist were blind to each other's findings and also to the findings of the health survey team.

We used four categorical independent variables relating to housing conditions. Households that received a house conditions survey were classified into three groups: those where there was no objective evidence of dampness or mould growth (dry), those with only damp, and those with mould (whether or not dampness was also present). The overall dampness in the household was calculated by averaging the score for each bedroom, sitting room, and kitchen on a four point scale of severity (0 = none; 3 = severe). Households in which the average dampness score exceeded zero (no dampness whatsoever) were divided into three approximately equal sized groups labelled mild (score ranging between 0.01 and 0.52), moderate (0.53 to 1.05), and severe ( $\geq 1.06$ ). A similar procedure was adopted to divide households into four groups differing in average severity of mould (none, mild (0.01 to

0.45), moderate (0.46 to 0.77), and severe ( $\geq 0.78$ )).

The spore concentration per m<sup>3</sup> air was measured in the kitchen, living room, and bedrooms of households in Edinburgh and Glasgow visited by the surveyors. On the basis of preliminary work in Edinburgh (B. Flanagan and C. A. Hunter, unpublished data) and elsewhere<sup>14</sup> we devised a five point scale (coded 1 to 5): low ( $\leq 100$  viable spores/m<sup>3</sup> air), medium (101-300), high (301-1000), very high (1001-5000), and extremely high ( $> 5000$ ). The household spore concentration was the mean score on the scale per available room. A new variable was created by dividing this mean score into three groups: low (scoring 1), medium (1.01 to 2.00), and high ( $> 2$ ).

To ensure that the relation between housing conditions and ill health was not invalidated by covariation with other variables several possible confounding factors were also examined, particularly cigarette smoking in the household (no/yes), respondents' cigarette smoking (no/yes), net household income (above median (£80)/below median), overcrowding (less than/more than 1.5 people per room), employment in the household (somebody employed/nobody employed), and employment state of the respondent (employed/unemployed, no paid employment).

The respondent was asked to report on the presence of 16 specific symptoms seen in the past two weeks in any child (aged 0-15) living in the household. We devised two summary symptom scores relating to children: the unadjusted score being the total number of symptoms among all children in the household and the adjusted score being the total of symptoms divided by the number of children—that is, the mean number of symptoms per child. Another summary dependent variable for children was the mean score on health evaluation derived from the respondent's general evaluation of each child on a scale of 1 (excellent) to 5 (very poor). The respondent was also asked to report whether she had suffered from any of 17 specific symptoms over the past fortnight. A summary symptom score was merely the sum of individual symptoms. In addition, the respondent was asked to rate her general health on the same five point scale used for children and to complete the 30 item general health questionnaire (range 0-30), here used as a general indicator of psychological distress. Finally, we inquired about medical treatment for symptoms and the presence of a recurrent or longstanding illness among both respondents and children.

Univariate analyses of the relation between each independent variable and dependent variables were carried out with  $\chi^2$  tests (categorical variables) or one way analysis of variance (metric variables). Subsequently, multivariate analyses were performed to examine the association between housing conditions and ill health after controlling for possible confounding factors. When the response variable was binary/categorical we used logistic linear regression analysis<sup>15</sup>; for metric response variables we used analysis of covariance. The extent of any dose-response relation between severity of dampness, mould growth, and air spore concentration and health was assessed by means of tau c (categorical variables) and the Pearson correlation coefficient (metric variables). Identical results were obtained with respect to metric variables transformed to base 10 logarithms. Only original values are reported below.

On the basis of previous work we expected to find a distinct effect of adverse housing conditions on respiratory and gastrointestinal symptoms in children and on emotional distress in adults. Evidence of a dose response relation was considered to be particularly relevant in assessing the likelihood of a causal impact of dampness and mould on symptomatic health.

For the purposes of this report the results from

2023379813

Edinburgh, Glasgow, and London have been combined. (Although the prevalence of damp and mould varied in each city, there were no pronounced differences in the association between housing conditions and symptomatic health state between cities.)

## Results

### RATES OF RESPONSE

Of 1220 households with children eligible for inclusion in the study, a health interview was secured in 891 (73.0%); 156 (12.8%) respondents refused to be interviewed, and 173 (14.2%) could not be contacted. Surveyors completed their investigations of housing conditions in 597 households, constituting 48.9% of eligible households and 67.0% of those who had the health interview. A comparison between surveyed ( $n=597$ ) and non-surveyed ( $n=294$ ) households showed no differences in sociodemographic characteristics, such as gender, marital state, household size (including number of children), social class, and overcrowding; or regarding disposable income, cigarette smoking, length of time at current address, presence of pets, or self-reported damp or mould. The only significant difference concerned employment: 131 (22%) respondents in surveyed households were employed compared with 100 (34%) respondents in non-surveyed households ( $\chi^2=12.54$ ,  $df=1$ ,  $p<0.001$ ); corresponding figures for any adult in employment were 257 (43%) and 156 (53%), respectively ( $\chi^2=7.55$ ,  $df=1$ ,  $p<0.01$ ).

All subsequent analyses were based on the 597 households, containing 1169 children, that received both a housing survey and a health interview.

### COMPARISON OF THREE HOUSING CONDITIONS GROUPS

Out of the 597 households, only 184 (30.8%) were free from damp or mould (dry). In 139 (23.3%) households surveyors found evidence of damp and in 274 (45.9%), of which all but nine were also damp; actual mould growth was visible. The three housing conditions groups (dry, only damp, mouldy) were compared for descriptive purposes on a number of background (sociodemographic and other) variables. (It was, of course, recognised that a variable could act as a confounder even if it did not differentiate significantly between groups.) Only one significant difference emerged: respondents living in dry households had been living an average of 5.9 (SD 4.9) years at the address compared with 4.8 (4.1) years among respondents in damp houses and 6.4 (5.5) years among

respondents in mouldy houses ( $F=4.35$ ,  $df=2, 584$ ,  $p<0.02$ ); only the difference between damp and mouldy houses was significant (Scheffe test,  $p<0.05$ ). Housing groups did not differ in number of children (mean (SD) 2.0 (1.0)), total number of household members (3.8 (1.2)), respondent's gender (559 (93.6%) women); respondent's marital state (384 (64.3%) married), net household income (293 (49.0%) under £80 per week), respondent's smoking (415 (69.5%)), any smoker in household (476 (79.7%)), respondent employed (136 (22.8%)), any household member employed (259 (43.4%)), overcrowding (109 (18.3%)), presence of pets (269 (45.1%)), tenure of last house (465 (77.9%) council dwelling), reasons for moving from last dwelling (90 (15.0%) because of dampness; 247 (41.4%) because of other problems with the house; 26 (4.3%) for health reasons), and use of Calor gas heating (81 (13.5%)). Respondents in mouldy households, however, reported more problems apart from the damp (especially noise, poor repair, and cold) than respondents in damp or dry households. (Mean (SD) problems 2.7 (1.5), 2.5 (1.6), and 2.2 (1.6), respectively;  $F=5.0$ ,  $df=2, 594$ ,  $p<0.01$ ). In particular, the prevalence of cold as a problem was reported in 222 (81%), 100 (72%), and 114 (62%) households, respectively;  $\chi^2=20.4$ ,  $df=2$ ,  $p<0.001$ ).

### HOUSING CONDITIONS AND RESPONDENT'S HEALTH

Table 1 shows the relation between prevalence of symptoms in the respondent and housing conditions. Significant differences between groups were found regarding bad nerves, aching joints, nausea and vomiting, backache, blocked nose, fainting spells, constipation, and breathlessness. The lowest proportion reporting symptoms was found in dry households; with only one exception (fainting spells) the highest proportion was found in mouldy households. Although housing conditions were unrelated to the presence of any particular symptom, there was a significant variation in the total number of symptoms and in the respondent's evaluation of her health. In particular, those living in mouldy houses scored significantly higher than those living in dry conditions (Scheffe test,  $p<0.05$ ). The general health questionnaire score was not related to housing conditions (table 1).

Preliminary univariate analyses had shown that only two of the possible confounding variables (respondent's economic position and cigarette smoking) were significantly associated with the presence or absence of individual symptoms. We therefore undertook a series of logistic regression analyses in which the dependent variables were the eight symptoms previously shown to be significantly associated with housing conditions. After controlling for the respondent's economic position and cigarette smoking these differences remained significant for all eight dependent symptom variables (problem free households always having the lowest proportion of respondents positive for symptoms).

The relation between housing conditions on the one hand and the total number of symptoms, health evaluation score, and general health questionnaire score on the other was further examined by means of analyses of covariance. After we controlled for length of time at address, other housing problems (or cold alone), respondent's economic position, respondent's cigarette smoking, and household income housing conditions remained significantly associated with the total number of symptoms (6 ranging between 0.10 and 0.14;  $p<0.05$  to  $<0.005$ ), with those living in mouldy households reporting most and those in dry households fewest symptoms. Housing conditions were not significantly associated with health evaluation score after we controlled for other possible con-

TABLE 1—Respondent's health during past two weeks by housing conditions. Figures are numbers (percentages) unless stated otherwise.

Symptom	Housing conditions			Significance		
	No damp or mould (n=184)	Damp only (n=139)	Mould (n=274)	$\chi^2$	Degrees of freedom	p Value
Tiredness	76 (41.3)	69 (50.0)	141 (51.5)	4.84	2	0.089
High blood pressure	9 (4.9)	7 (5.1)	22 (8.0)	2.33	2	0.312
Persistent cough	30 (16.3)	27 (19.4)	64 (23.4)	3.47	2	0.177
Bad nerves	35 (19.0)	31 (22.3)	80 (29.2)	6.62	2	0.036
Wheezing	19 (10.3)	17 (12.2)	37 (13.6)	1.07	2	0.587
Aching joints	28 (15.2)	23 (16.5)	65 (23.7)	6.05	2	0.049
Skin problems	26 (14.1)	23 (16.5)	43 (15.7)	0.39	2	0.825
Persistent headaches	49 (26.6)	43 (30.9)	75 (27.4)	0.82	2	0.664
Nausea/vomiting	7 (3.8)	9 (6.5)	27 (9.9)	6.17	2	0.046
Backache	41 (22.3)	48 (34.5)	81 (29.6)	6.13	2	0.047
Blocked nose	25 (13.6)	18 (12.9)	58 (21.2)	6.53	2	0.038
Palpitations	8 (4.3)	9 (6.5)	22 (8.0)	2.44	2	0.295
Fainting spells	3 (1.6)	12 (8.6)	17 (6.2)	8.37	2	0.015
Diarrhoea	5 (2.7)	9 (6.5)	19 (6.9)	4.06	2	0.131
Constipation	11 (6.0)	8 (5.8)	33 (12.0)	7.08	2	0.029
Breathlessness	19 (10.3)	24 (17.3)	51 (18.6)	6.01	2	0.049
Feeling depressed	51 (27.7)	47 (33.8)	104 (38.0)	5.15	2	0.076
Any symptom	144 (78.3)	113 (81.3)	217 (79.2)	0.46	2	0.795
Mean SD No of symptoms	2.40 (2.37)	3.05 (3.01)	3.43 (3.25)	$F=6.67$	2, 594	0.001
Mean SD health evaluation score	2.41 (0.93)	2.49 (0.99)	2.66 (0.97)	$F=4.09$	2, 594	0.017
Mean SD general health questionnaire score	5.74 (7.12)	6.87 (7.78)	7.20 (8.35)	$F=1.92$	2, 583	0.148

founding variables, and the relation with the general health questionnaire score remained non-significant.

We examined the dose-response relation between the respondents' symptoms and increasing severity of dampness, mould growth, and air spore concentration. Table II summarises the findings of these analyses.

TABLE II—Respondent's health during past two weeks: Dose-response relation with damp, mould, and air spore count. Figures are tau  $\tau$  values ( $p$  values) unless stated otherwise

Symptom	Dampness (Max n=597)	Mould growth (Max n=589)	Air spore count (Max n=485)
Tiredness	0.09 (0.028)	0.06 (0.076)	-0.02 (0.341)
High blood pressure	0.04 (0.024)	0.04 (0.027)	0.05 (0.017)
Persistent cough	0.09 (0.010)	0.04 (0.110)	0.06 (0.062)
Bad nerves	0.07 (0.036)	0.09 (0.008)	0.08 (0.031)
Wheezing	0.05 (0.047)	0.03 (0.125)	0.01 (0.413)
Aching joints	0.05 (0.080)	0.07 (0.022)	0.06 (0.083)
Skin problems	0.03 (0.209)	0.00 (0.474)	0.06 (0.063)
Persistent headaches	0.04 (0.150)	-0.02 (0.279)	-0.11 (0.006)
Nausea/vomiting	0.04 (0.044)	0.05 (0.015)	0.02 (0.230)
Backache	0.04 (0.167)	0.02 (0.332)	0.11 (0.009)
Blocked nose	0.11 (0.001)	0.08 (0.005)	0.00 (0.451)
Palpitations	0.03 (0.096)	0.03 (0.051)	0.08 (0.001)
Fainting spells	0.05 (0.013)	0.01 (0.381)	-0.01 (0.289)
Diarrhoea	0.02 (0.146)	0.02 (0.109)	-0.01 (0.413)
Constipation	0.02 (0.271)	0.04 (0.054)	0.01 (0.414)
Breathlessness	0.09 (0.003)	0.05 (0.057)	0.08 (0.019)
Feeling depressed	0.06 (0.081)	0.08 (0.026)	0.06 (0.107)
Any symptom	0.02 (0.319)	-0.02 (0.299)	0.00 (0.482)
No of symptoms	$r=0.14$ (0.001)	$r=0.09$ (0.014)	$r=0.08$ (0.039)
Health evaluation score	$r=0.07$ (0.047)	$r=0.10$ (0.008)	$r=0.05$ (0.115)
General health questionnaire	$r=0.06$ (0.082)	$r=0.06$ (0.086)	$r=0.01$ (0.414)

There was a significant tendency for increasing severity of dampness to be associated with a greater prevalence of the following symptoms: tiredness, high blood pressure, persistent cough, bad nerves, wheezing, nausea and vomiting, blocked nose, fainting spells, and breathlessness. The greater the extent of mould growth the higher the proportion of respondents reporting high blood pressure, bad nerves, aching joints, nausea and vomiting, blocked nose, and feeling depressed. Finally, the concentration of the air spores was positively associated with high blood pressure, bad nerves, backache, palpitations, and breathlessness and negatively associated with persistent headaches. Overall, the total number of symptoms tended to increase with higher degrees of dampness and mould and air spore concentration, while the health evaluation score was related only to severity of dampness and mould growth. No dose-response effect on the general health questionnaire score was evident.

Respondents living in the three different housing conditions were compared regarding action taken

during the past two weeks to deal with symptoms and presence of recurrent and long-standing illness. No significant differences were found.

#### HOUSING CONDITIONS AND CHILDREN'S HEALTH

Table III shows the prevalence of symptoms among children in the household by housing conditions. Significant differences were found regarding wheezing, sore throat, persistent headache, fever and high temperature, persistent cough, and runny nose. The highest proportion reporting these symptoms was always found in mouldy households; with only one exception (sore throat) the lowest proportion with symptoms was found in the dry households. Not only was there a significant difference in the proportion with any symptom (147 (79.9%) in dry households, 119 (85.6%) in damp houses, 248 (90.5%) in mouldy houses) but the mean number of symptoms (overall and per child) also differed significantly and in the same direction. The mean child health evaluation score was not significantly different between groups (table III).

In our preliminary univariate analyses we had noted that three of the possible confounding variables (overcrowding, any cigarette smoker, nobody employed) were significantly associated with presence or absence of individual symptoms. Another set of logistic regression analyses was therefore undertaken in which the dependent variables were the six symptoms previously shown to be significantly associated with housing conditions. After controlling for these three confounding variables differences remained significant for wheezing, sore throat, persistent headache, fever and high temperature, runny nose, and for any symptom. Only the main effect of housing conditions on cough was no longer significant.

The relation between housing conditions on the one hand and mean number of symptoms and mean health evaluation score on the other was further examined in a series of analyses of covariance. As before, we took into account differences in the length of time at address and other housing problems (or cold alone). We also added a control for the number of children in the household and the adult's general health questionnaire score (included because although it did not differ significantly with housing conditions, it was correlated highly with both the mean number of symptoms in children ( $r=0.30$ ,  $p<0.001$ ) and mean child health evaluation score ( $r=0.35$ ,  $p<0.001$ )). Finally, we partialled out the effects of cigarette smoking in the household, unemployment, low income, and overcrowding. There was still a significant effect of housing conditions on the mean number of symptoms (6 ranging between 0.10 and 0.13,  $p<0.02$  to  $<0.005$ ). Children living in mouldy households were reported to have the highest number of symptoms and those living in dry households the fewest. Mean child health evaluation score remained unrelated to housing conditions.

Table IV shows the dose-response relation between children's symptoms and increasing severity of dampness, mould growth, and air spore concentration. The more serious the dampness the greater the prevalence of bodily aches and pains, wheezing, vomiting, sore throat, irritability, tiredness, persistent headache, fever and high temperature, feeling depressed and unhappy, poor appetite, persistent cough, and runny nose. Dampness was also associated overall with the presence of any symptom. The more severe the mould growth the greater the likelihood of wheezing, sore throat, irritability, persistent headache, fever and high temperature, and runny nose. Mould growth was also associated with the presence of any symptom. The greater the air spore concentration the greater the prevalence of wheezing, irritability, and fever and high temperature.

TABLE III—Children's health during past two weeks by housing conditions. Figures are number (percentages) unless stated otherwise

Symptom*	Housing conditions			Significance		
	No damp or mould (n=184)	Damp only (n=139)	Mould (n=274)	Degrees of freedom	$\chi^2$	$p$ Value
Bodily aches/pains	23 (12.5)	30 (21.6)	43 (15.7)	4.90	2	0.086
Diarrhoea	34 (18.5)	30 (21.6)	50 (18.2)	0.73	2	0.694
Wheezing	30 (16.3)	26 (18.7)	74 (27.0)	8.41	2	0.015
Vomiting	22 (12.0)	25 (18.0)	52 (19.0)	4.18	2	0.124
Sore throat	56 (30.4)	34 (24.5)	116 (42.3)	14.99	2	<0.001
Irritability	23 (12.5)	28 (20.1)	56 (20.4)	5.32	2	0.070
Tiredness	25 (13.6)	28 (20.1)	48 (17.5)	2.55	2	0.279
Persistent headaches	23 (12.5)	19 (13.7)	58 (21.2)	7.16	2	0.028
Earache	27 (14.7)	15 (10.8)	47 (17.2)	2.95	2	0.228
Fever/high temperature	21 (11.4)	25 (18.0)	67 (24.5)	12.30	2	0.002
Feeling depressed/unhappy	20 (10.9)	25 (18.0)	42 (15.3)	3.45	2	0.178
Temper tantrums	37 (20.1)	37 (26.6)	74 (27.0)	3.13	2	0.209
Bedwetting	41 (22.3)	29 (20.9)	64 (23.4)	0.33	2	0.846
Poor appetite	31 (16.8)	37 (26.6)	68 (24.8)	5.49	2	0.064
Persistent cough	57 (31.0)	52 (37.4)	117 (42.7)	6.45	2	0.040
Runny nose	72 (39.1)	56 (40.3)	139 (50.7)	7.43	2	0.024
Any symptom	147 (79.9)	119 (85.6)	248 (90.5)	10.41	2	0.006
Mean (SD) No of symptoms	3.73 (3.95)	4.39 (4.63)	5.44 (5.19)	F=7.56	2,594	<0.001
Mean (SD) No of symptoms per child	2.04 (1.98)	2.46 (2.36)	2.86 (2.43)	F=7.23	2,594	<0.001
Mean (SD) health evaluation score	2.24 (0.89)	2.30 (0.91)	2.41 (0.94)	F=1.98	2,592	0.140

\*Symptom present in any child living in household.

TABLE IV—Children's health during past two weeks. Dose-response relation with damp, mould, and air spore count. Figures are tau  $\tau$  values ( $p$  values) unless stated otherwise

Symptom	Dampness (Max n=597)	Mould growth (Max n=589)	Air spore count (Max n=485)
Bodily aches-pains	0.08 (0.006)	-0.01 (0.383)	-0.01 (0.384)
Diarrhoea	0.02 (0.291)	-0.01 (0.386)	0.01 (0.361)
Wheezing	0.10 (0.005)	0.09 (0.005)	0.07 (0.044)
Vomiting	0.06 (0.029)	0.04 (0.106)	0.03 (0.238)
Sore throat	0.09 (0.020)	0.14 (<0.001)	0.03 (0.264)
Irritability	0.10 (0.004)	0.06 (0.040)	0.07 (0.033)
Tiredness	0.06 (0.043)	0.01 (0.365)	0.01 (0.351)
Persistent headaches	0.12 (<0.001)	0.09 (0.002)	0.00 (0.456)
Ears-ache	-0.01 (0.349)	0.03 (0.170)	-0.04 (0.130)
Fever-high temperature	0.12 (<0.001)	0.10 (0.002)	0.06 (0.046)
Feeling depressed-unhappy	0.08 (0.007)	0.02 (0.237)	-0.02 (0.294)
Temper tantrums	0.04 (0.159)	0.06 (0.069)	0.01 (0.399)
Bedwetting	0.02 (0.313)	0.00 (0.460)	-0.01 (0.437)
Poor appetite	0.08 (0.015)	0.03 (0.200)	0.02 (0.336)
Persistent cough	0.11 (0.006)	0.06 (0.068)	0.05 (0.139)
Runny nose	0.08 (0.033)	0.09 (0.023)	0.06 (0.123)
Any symptom	0.08 (0.005)	0.07 (0.011)	0.00 (0.492)
Mean No of symptoms	$r=0.17$ (0.001)	$r=0.14$ (0.001)	$r=0.11$ (0.010)
Mean No of symptoms per child	$r=0.13$ (0.001)	$r=0.12$ (0.002)	$r=0.05$ (0.161)
Mean health evaluation score	$r=0.08$ (0.025)	$r=0.07$ (0.044)	$r=0.06$ (0.107)

Overall, the mean number of symptoms tended to increase with greater severity of dampness, mould growth, and air spore concentration, whereas the mean number of symptoms per child and the mean child health evaluation score were related only to greater doses of dampness and mould growth. The mean number of symptoms per child and the mean child health evaluation score were unrelated to the extent of air spore concentration.

The three groups of housing conditions were compared regarding the action taken to deal with children's symptoms during the past two weeks and presence of recurrent and longstanding illness. Children in mouldy households were more likely to have been given medicines (51.8%) than children in damp (43.2%) or problem free households (36.4%) ( $\chi^2=10.82$ ,  $df=2$ ,  $p<0.005$ ). Other differences did not reach significance.

## Discussion

Before offering an account of the role of damp and mould in the aetiology of symptoms it is necessary to consider four types of bias that may invalidate the assumption of a causal link between housing conditions and ill health—namely, investigator bias, respondent bias, selection bias, and omitted variable bias.

Investigator bias may be dismissed as housing conditions and the health of household members were independently assessed by two different groups of researchers, neither of which included the principal investigators. In addition, questionnaires were coded and data prepared by workers who were not familiar with the objectives of the study.

Some previous investigations of the housing-health relation, particularly those carried out by tenants' groups, have been criticised on the grounds that people living in damp and mouldy houses will be inclined to exaggerate the extent of their own and their children's health problems. A recent study suggested that the observed association between mould and respiratory symptoms may be accounted for by parental awareness of mould in the home.<sup>1</sup> Our reliance on informants' reports about the health of themselves and their children was deliberate. We were unconvinced about the reliability and appropriateness of diagnostic data derived from official records, especially those of general practitioners. We thought that it was valid to assess health state by means of self reported symptoms while at the same time recognising that the likelihood of respondent bias was thereby increased. This

problem was minimised, however, by the use of independent, expert assessments of housing conditions. Although subjective (self reported) and objective (expert) evaluations of the presence of damp and mould were significantly and positively associated ( $k=0.26$ ,  $p<0.001$ ), there was disagreement about damp and mould state in 183 (30.7%) of the dwellings. Furthermore, respondents could not have been aware of the air spore concentration in the building. (The association between self reported damp mould and spore count, although significant, was not high:  $r=0.14$ ,  $p<0.001$ .) Nevertheless, symptoms in both children and respondents were related to this measure. We also included the general health questionnaire score as a covariate when examining the effect of housing conditions among children as respondents with greater levels of psychological distress tended to report more ill health. The mean number of symptoms remained significantly higher in damp and mouldy dwellings than in dry dwellings. Thus though the overall number of symptoms may have been higher than would be obtained by an independent observer, there is no reason to believe that such a bias affected the main findings.

Another possible source of error is that of selection bias. People who already suffer from ill health may tend to live in damp or mouldy dwellings: symptoms may exist before, rather than be a consequence of, living in poor housing conditions. This could happen, for example, where the least desirable dwellings were allocated to those most in need who, by virtue of low income, social circumstances, or medical history, were more likely to report ill health. Although housing departments may not always act impartially in the selection of tenants to households, there is no evidence to suggest that they systematically allocate families in poorer health to damp and mouldy households. In this study families in damp and mouldy dwellings were not more likely to have come from previously poor conditions or to have moved for health reasons or to have lived a shorter period of time in the dwelling than families in dry houses. In addition, many of the children in all three housing groups were born in the household in which they were currently living. Thus selection bias is highly unlikely to account for the findings.

Omitted variable bias can arise when variables that are correlated with the major independent variable (in this case housing conditions) and have a significant (possibly causal) relation with the dependent (outcome) variable (such as symptom score) are excluded from the analysis. Whereas several factors were significantly associated with health state, only cold was also associated with housing conditions. Cold stress may have made some contribution to the experience of symptoms: a damp house is usually a cold house. Unfortunately, we were unable to assess the temperature of dwellings. We did, however, gather information on perceived coldness of the dwelling and this variable was included in the covariance analysis.

In summary, adult respondents living in damp and mouldy dwellings were more likely to report nausea, vomiting, constipation, blocked nose, breathlessness, backache, aching joints, fainting, and bad nerves than respondents living in dry dwellings. These differences remained after controlling for the respondent's economic position and cigarette smoking. In a more extensive covariance analysis respondents living in mouldy dwellings were found to have the highest number of symptoms even after taking account of possible confounding factors such as length of time at address, other housing problems, household income, economic position, and cigarette smoking. This analysis, however, showed that the respondent's subjective evaluation of health and psychological distress

2023379816



were both unrelated to housing conditions. Increasing doses of dampness and mould were especially linked to nausea, blocked nose, breathlessness, high blood pressure, and bad nerves and to a greater number of symptoms and a poorer health evaluation score.

For children, living in damp and mouldy dwellings was associated with a greater prevalence of wheeze, sore throat, runny nose, cough, headaches, and fever compared with those living in dry dwellings. With the exception of cough these differences were unaffected by the introduction of controls for smoking in the household, employment, and overcrowding. Additional possible confounding variables were added in an analysis of covariance, which still showed a significant effect of housing conditions on the mean number of symptoms among children in the household. A dose-response relation was particularly noted with respect to wheeze, sore throat, runny nose, irritability, persistent headache, and fever and high temperature. Increasing severity of dampness and mould and any symptom, the mean number of symptoms (overall and per child), and the mean child health evaluation score were also associated.

Several studies have suggested that some varieties of fungal spores are allergenic and give rise to respiratory conditions. Burr *et al* identified *Penicillium notatum*, *Cladosporium herbarum*, and *Aspergillus* species in the homes of asthmatic patients and found that the moulds gave positive skin test reactions for allergy.<sup>1</sup> Fungal spores are also believed to affect the respiratory tract by producing tissue lesions, by forming saprophytic colonies on mucus plugs, and by causing inflammation and irritation of nasal and bronchial passages and the alveoli.<sup>10,11</sup>

An investigation by May *et al* found symptoms of fever, muscular pain, chest tightness, cough, and headache to be directly caused by organic toxic dust and suggested that this "pulmonary mycotoxicosis" may represent a systemic reaction to inhaled fungal toxins.<sup>12</sup> Although their study was concerned with acute episodes after exposure to massive doses of organic dust, possibly similar, though less severe, symptoms occur as a chronic response to prolonged exposure to low concentrations of fungal toxins.

Analysis of the moulds collected from the dwellings in our study is still proceeding and a supplementary report on the relation of specific moulds to symptoms will be prepared. Single dwellings in the study were found to be harbouring over 15 species of mould and probably some of these would give rise to allergenic or toxic reactions, or both.

Emotional symptoms in children such as irritability and unhappiness are probably linked to physical symptoms and indicate that the mental health of children is also at risk. Some of the adults' symptoms are difficult to explain by reference to mould, though aching joints and nausea could both be reactions to fungal toxins. Reports of "bad nerves" are not surprising where living areas are unpleasant, children are sick, and family life may be fraught. Backache and constipation are puzzling phenomena and may be indirect consequences of conditions in the home. Breathlessness and blocked nose may be more closely related to low temperature. Increased blood pressure and hypoxia have been observed as reactions to cold stress.<sup>13</sup>

We have attempted at all stages of this study, which is probably the largest of its kind ever undertaken, to refute the null hypothesis—namely, that there is no relation between housing conditions and health state. To that end, we adopted double-blind interviewing procedures, included a wide array of possible confounding factors, and used multivariate statistical techniques. Having eliminated (as far as possible, alternative explanations for our findings, we concluded that damp and mouldy dwellings have direct deleterious effects on the physical and psychological well-being of adults and children. Our confidence in this conclusion is enhanced in more positive fashion by two observations: firstly, the similarity of these findings with those reported in our earlier study,<sup>1</sup> especially concerning children's respiratory symptoms; and, secondly, the strong relation between increasing doses of adverse housing conditions (dampness, mould growth, and air spore concentration) and symptoms of ill health, which is unlikely to be the result of respondent bias.

A considerable body of evidence now exists that supports the contention that dampness and mould is an important public health issue, not solely for its immediate impact but also for the longterm implications. Poor housing conditions in childhood, for example, are associated with higher rates of admission to hospital and higher morbidity and mortality in adult life.<sup>14</sup> Hopefully, planners, policy makers, and medical practitioners will now plan concerted joint action to eradicate this unacceptable and needless health risk.

This study was supported by grants from Glasgow and Edinburgh district councils and the London Research Centre. Many associations and people have contributed to this research. In particular, we acknowledge advice and practical assistance from the Community Health Resource Unit, Glasgow; Easthall Residents' Association; Royston, Molendinar community councils, and the Technical Services Agency, Glasgow.

1. Martin CJ, Platt SD, Hunt SM. Housing conditions and ill health. *Br Med J* 1987;294:1125-7.
2. Institute of Environmental Health Officers. *Mould fungal spores—their effects on health and the control, prevention and treatment of mould growth in dwellings*. London: IEHO, 1985.
3. Gravesen S. Fungi as a cause of allergic disease. *Allergy* 1979;34:135-54.
4. Larsen LS. A three year survey of microfungi in the air of Copenhagen 1977-1979. *Allergy* 1981;36:15-22.
5. Goldberg DP. *The detection of psychiatric illness by questionnaire*. London: Oxford University Press, 1972.
6. Baker RJ, Nelder JA. *The GLIM system manual Release 3*. Oxford: Numerical Algorithms Group, 1978.
7. SPSS. *SPSS-X user's guide*. New York: McGraw-Hill, 1983.
8. Strachan DP. Damp housing and childhood asthma: validation of reporting of symptoms. *Br Med J* 1988;297:1123-6.
9. Burr ML, Mullins J, Merrett TG, Scott NC. Indoor moulds and asthma. *J Roy Soc Health* 1988;3:99-101.
10. Hosen H. Moulds in allergy. *Journal of Asthma Research* 1978;15:151-6.
11. Maunsell K. Sensitisation risk from inhalation of fungal spores. *J Laryngol Otol* 1954;68:765-75.
12. May JJ, Stallones L, Darrow D, Pratt DS. Organic dust toxicity: pulmonary mycotoxicosis associated with silo unloading. *Thorax* 1986;41:919-23.
13. Lloyd E. Cold stress and ischaemic heart disease. *Radical Community Medicine* 1987;30:9-11.
14. Folmer-Anderson T. Persistence of social and health problems in the welfare state: a Danish cohort experience from 1948 to 1979. *Soc Sci Med* 1984;18:555-60.
15. Britten N, Davies JMC, Colles JRT. Early respiratory experience and subsequent cough and peak expiratory flow rate in 36 year old men and women. *Br Med J* 1987;294:1317-20.

(Accepted 29 April 1989)

2023379817

2023379818

Bruneekreef, B., Dockery, D.W., Speizer, F.E., Ware, J.H., Spengler, J.D., Ferris, B.G. "Home Dampness and Respiratory Morbidity in Children" American Review of Respiratory Disease 140: 1363-1367, 1989.

SUMMARY: This study examined the relationship between measures of home dampness and respiratory illness and symptoms in a cohort of 4,625 eight-to 12-yr-old children living in six U.S. cities. Home dampness was characterized from questionnaire reports of mold or mildew inside the home, water damage to the home, and the occurrence of water on the basement floor. Symptoms of respiratory and other illness were collected by questionnaire. Pulmonary function was measured by spirometry. Signs of home dampness were reported in a large proportion of the homes. In five of the six cities, one or more of the dampness indicators were reported in more than 50% of the homes. The association between measures of home dampness and both respiratory symptoms and other non-chest illness was both strong and consistent. Odds ratios for molds varied from 1.27 to 2.12, and for dampness from 1.23 to 2.16 after adjustment for maternal smoking, age, gender, city of residence, and parental education. The relationship between home dampness and pulmonary function was weak, with an estimated mean reduction of 1.0% in FEF25-75 associated with dampness and 1.6% with molds. We conclude that dampness in the home is common in many areas of the United States and that home dampness is a strong predictor of symptoms of respiratory and other illness symptoms among 8- to 12-yr-old children.

2023379819

# Home Dampness and Respiratory Morbidity in Children<sup>1-4</sup>

BERT BRUNEKREEF,<sup>\*</sup> DOUGLAS W. DOCKERY,<sup>\*</sup> FRANK E. SPEIZER, JAMES H. WARE,  
JOHN D. SPENGLER, and BENJAMIN G. FERRIS

## Introduction

Dampness in the home is a potential risk factor for respiratory illness in part through the action of (micro)organisms that thrive in damp environments. Dust mites (Pyroglyphidae) are a well-known source of allergenic substances (1-5). They thrive at relative humidities greater than 70%, and they are found in mattresses, carpets, and dust on surfaces moist enough to support them. Dust mites are most abundant at the end of the summer, after a prolonged period of high indoor humidity (6-10). They can survive low humidity conditions to a certain extent, but their numbers are reduced significantly in homes that are very dry in winter (10). The prevalence of mites and allergens in house dust decreases with increasing altitude (1, 11, 12), presumably because wintertime humidity is lower at higher altitudes. Few mites are found in dusts obtained in dry climates (13, 14). Murray and coworkers (15) reported a 10- to 20-fold increase in sensitization to mite extracts in children living in a damp climate when compared with children living in a dry climate. Sensitization to cat and dog dander was comparable to the two groups. Long before the house dust mite was shown to be responsible for allergy to house dust (1), it was known that asthmatics normally living at low altitudes suffered far fewer attacks at high altitudes, and that asthmatic patients generally had negative skin tests for dusts collected at high altitudes (16). Recently, an increased prevalence of asthma in Papua, New Guinea, has been associated with the increased use of blankets containing large numbers of dust mites (17).

Molds are another source of respiratory allergens (18-21). Mold species have critical relative humidities ranging from less than 80% to more than 90% (18). Some genera have stronger allergenic properties than do others, and within a genus, there can be considerable variation in allergenic potential among species (21). Mold growth in homes can cause severe respiratory disease requiring hos-

**SUMMARY** This study examined the relationship between measures of home dampness and respiratory illness and symptoms in a cohort of 4,825 eight- to 12-yr-old children living in six U.S. cities. Home dampness was characterized from questionnaire reports of mold or mildew inside the home, water damage to the home, and the occurrence of water on the basement floor. Symptoms of respiratory and other illness were collected by questionnaire. Pulmonary function was measured by spirometry. Signs of home dampness were reported in a large proportion of the homes. In five of the six cities, one or more of the dampness indicators were reported in more than 50% of the homes. The association between measures of home dampness and both respiratory symptoms and other non-chest illness was both strong and consistent. Odds ratios for molds varied from 1.27 to 2.12, and for dampness from 1.23 to 2.16 after adjustment for maternal smoking, age, gender, city of residence, and parental education. The relationship between home dampness and pulmonary function was weak, with an estimated mean reduction of 1.0% in FEF<sub>75-75</sub> associated with dampness and 1.8% with molds. We conclude that dampness in the home is common in many areas of the United States and that home dampness is a strong predictor of symptoms of respiratory and other illness symptoms among 8- to 12-yr-old children.

AM REV RESPIR DIS 1989; 140:1363-1367

pitalization (22-24). Typical causes of abundant mold growth include leaks in the roofs or walls, urinating pets, improper carpet cleaning, leaky plant pots, and the use of a cold mist vaporizer (22-24). Molds are ubiquitous in ambient air, and in dry homes, the presence of molds appears mainly to be related to their presence in outdoor air (25). *Penicillium* and *Aspergillus* are among the molds typically found in residences (26-31). Within the allergic population, the prevalence of mold allergy has been estimated to be 2 to 30% (32).

Despite this information about the potentially harmful effects of home dampness on respiratory health, relatively few epidemiologic studies have investigated the health effects of dampness. A study from the United Kingdom reported an association in a group of about 200 children between the prevalence of respiratory symptoms and relative humidity in their bedrooms (33). Lesourd and coworkers (34) reported a trend toward increasing prevalence of cutaneous delayed-type hypersensitivity to a battery of ubiquitous antigens in white, Hispanic, and black schoolchildren. These investigators attributed this trend to the increased risk of exposure to microorganisms in poorer homes. Varekamp and Voorhorst (35) and Leupen (36) reported that patients with bronchial asthma were

more likely to live in damp homes than were control subjects.

This report utilizes information on home characteristics and respiratory health of children participating in a large, ongoing epidemiologic study of air pollution

(Received in original form October 25, 1988 and in revised form April 17, 1989)

<sup>1</sup> From the Respiratory Epidemiology Program, Department of Environmental Science and Physiology, Harvard School of Public Health, and Channing Laboratory, Department of Medicine, Harvard Medical School, Brigham and Women's Hospital, Boston, Massachusetts.

<sup>2</sup> Supported in part by Grants ES-00002 and ES-01108 from the National Institute of Environmental Health Sciences, by Cooperative Agreement CR811650 from the Environmental Protection Agency, and by Contract RP-1001 from the Electric Power Research Institute.

<sup>3</sup> This report has not been subjected to the Environmental Protection Agency's required peer and policy review and therefore does not necessarily reflect the reviews of the agency, and no official endorsement should be inferred.

<sup>4</sup> Correspondence and requests for reprints should be addressed to Dr. Douglas W. Dockery, Respiratory Epidemiology Program, Harvard School of Public Health, 665 Huntington Ave., Boston, MA 02115.

<sup>5</sup> Recipient of a grant from the Netherlands Organization for the Advancement of Pure Research (ZWO).

<sup>6</sup> Recipient of a Faculty Development Award from the Mellon Foundation.

2023379820

and respiratory health to explore the relationship between moisture in the home and respiratory symptoms in children.

## Methods

### Study Population

The study population consists of 6,273 school-children living in six U.S. communities originally selected for their historic outdoor air pollution levels. These communities include Watertown, MA; Kingston and Harriman, TN; a geographically defined area in the southeast corner of St. Louis, MO; Steubenville and Mingo Junction, OH; Portage, Par-deeville, and Wyocena, WI, and a random sample of 50% of the schools in Topeka, KS.

Initially, approximately 1,000 children were enrolled in each city between 1983 (Watertown) and 1986 (Topeka). The cohort was drawn from the second through the fifth grades, with the number of grades depending on the size of the school population. Overall, 95.9% of the invited children participated. Sample sizes in participating communities varied between 832 (Watertown) and 1,135 (St. Louis). One year after the first examination, the children were invited to participate in a follow-up study. A total of 5,395 children participated, ranging from 735 in Watertown to 1,005 in Topeka. For 5,321 of these participants, both a questionnaire and a pulmonary function test were obtained. This report is based on the 4,625 white children who were 7 to 11 yr of age at the start of the study and who were seen again at the 1-yr follow-up examination.

### Health, Exposure, and Demographic Information

At both examinations, a questionnaire was given to each child to be completed by a parent or guardian and returned to school. Information regarding respiratory illnesses and symptoms was requested in a format equivalent to that recommended by the Epidemiology Standardization Project (37). Of the respiratory illnesses and symptoms, responses concerning doctor-diagnosed respiratory illness before 2 yr of age, bronchitis in the previous year, persistent cough (for 3 months of the year or more), persistent wheeze (most days or nights or apart from colds), chest illness that kept the child at home for 3 days or more, and an index of lower respiratory illness (bronchitis, cough, or chest illness) were considered. The questionnaire-based definition of these symptoms has been reported previously (38). In addition, the occurrence of doctor-diagnosed asthma in the past year has been considered, as home dampness appears to increase the presence of substances that cause and/or aggravate asthma. The occurrence of hay fever in the past year has been considered, as this may be indicative of the child's sensitivity to respiratory allergens. Other nonchest illnesses that restricted the child's activities for 3 days or more also were investigated, as molds may release biologically active substances that lead to systemic effects

(39). These other nonchest illnesses were defined by the question: "In the past year, has this child had any other major illness or accident that restricted his/her activities for a week or more?" This immediately followed the analogous question on chest illnesses.

The effect of home dampness on respiratory symptoms was evaluated separately for children with asthma or asthmatic symptoms. Persistent wheeze is often considered to be a marker for asthma in children. In this sample, more than half of the children with persistent wheeze did not report doctor-diagnosed asthma. Three groups of children were considered: children with doctor-diagnosed asthma, children with persistent wheeze but without doctor-diagnosed asthma, and children with neither asthma nor persistent wheeze.

In the initial as well as the follow-up questionnaire, information was asked about the family's smoking habits. Exposure to environmental tobacco smoke was expressed as the presence or absence of a mother who smokes in the home, a variable previously shown to affect childhood respiratory illness rates (38). Paternal smoking is highly correlated with maternal smoking, and it has been shown to affect childhood respiratory illness rates, although not as strongly as maternal smoking (38). Only maternal smoking was controlled in this analysis. The mean number of years of schooling of the parents (< 9, 9-12, > 12) was used as a proxy for socioeconomic factors that might influence respiratory health or symptom reporting.

The children were examined at school, where their weight and height in stockinged feet were measured. Forced expiratory maneuvers were performed on a recording spirometer (Survey Spirometer; Warren E. Collins, Braintree, MA) in a sitting position with free mobility without a noseclip. A detailed description of the measurement procedure has been given elsewhere (40).

In the follow-up questionnaire, three questions were included regarding potential moisture problems in the home: (1) Does water ever collect on the basement floor? (2) Has there ever been water damage to the building? (3) Has there ever been mold or mildew on any surface inside the home? From these, a fourth variable, home dampness, was created

(dampness absent if answers to questions 1 to 3 were negative, present if any were positive).

Indoor air pollution measurements, including humidity, were made in a stratified random sample of the homes of about 1,800 children (41). Relative humidity of the indoor air is less important for the growth of mites and fungi than the dampness of specific surfaces or parts of the building structure. These measurements will be reported separately.

The relationship between the questionnaire indicators of dampness and the respiratory health outcomes is the subject of this report.

### Statistical Methods

As a first step, symptom prevalences were calculated for each category of the home dampness variables. To investigate potential differences between cities, odds ratios were calculated for a number of relevant symptoms against the combined dampness variable for each city. In the next step, logistic regression models were constructed in which the association between home dampness variables and symptoms was adjusted for age, sex, parental education, maternal smoking, and city of residence.

Pulmonary function was measured by FEV<sub>1</sub>, FVC, and FEF<sub>25-75</sub>. The logarithm of each pulmonary function variable was regressed on an indicator of sex and on the logarithm of age, height, and weight plus maternal smoking, parental education, and indicator variables for the city of residence. Previously published analyses of pulmonary function of preadolescent children (40) have shown that this logarithmic transformation produces a linear relationship with constant variance. The residuals from these models were compared between categories of the home dampness variables by *t* test.

All statistical analyses were performed using the SAS Statistical Analysis System (42) on a Compaq 286 Deskpro personal computer.

### Results

Reporting rates for the different home dampness variables are given for each city in table 1. Molds and mildew were reported in almost 40% of homes in Kings-

TABLE 1  
REPORTING RATES FOR HOME DAMPNESS VARIABLES IN SIX U.S. CITIES

City	Reporting Rate for:			
	Molds (%)	Water Damage (%)	Basement Water* (%)	Dampness† (%)
Kingston, TN	38.1	12.1	11.3	45.7
Steubenville, OH	27.9	14.7	38.0	55.6
Watertown, MA	20.9	16.4	42.0	55.8
St. Louis, MO	26.9	23.0	39.4	56.4
Topeka, KS	33.0	22.2	30.0	56.9
Portage, WI	35.4	16.0	33.3	58.2

\* Includes homes with no basements.

† Dampness is defined as molds, water damage, or water in basement.

2023379821

TABLE 2  
SYMPTOM PREVALENCE FOR EACH OF THE HOME DAMPNES VARIABLE CATEGORIES:

Symptom	Dampness Variable							
	Molds		Water Damage		Basement Water		Dampness	
	Yes	No	Yes	No	Yes	No	Yes	No
Wheeze	14.8	8.9	15.0	9.9	11.2	10.4	12.2	9.0
Cough	11.7	6.1	10.9	7.2	9.6	7.1	10.1	5.1
Bronchitis	11.1	7.0	10.3	7.8	7.9	8.5	9.0	7.4
Chest illness	10.7	7.7	11.4	8.0	10.0	7.9	9.9	6.8
Lower respiratory illness	24.5	16.2	23.8	17.7	20.8	17.9	22.0	14.8
Respiratory illness before age 2	12.3	8.4	10.8	9.3	10.0	9.4	10.8	8.1
Asthma	5.4	4.4	5.4	4.5	5.2	4.5	5.1	4.1
Hay fever	23.2	15.8	22.2	17.4	19.4	17.6	19.8	16.3
Nonchest illness	12.5	9.1	13.7	9.5	11.7	9.6	11.9	8.3

ton/Harriman, TN. Reporting rates in other communities ranged from 20.9% in Watertown to 35.4% in Portage. A high rate of water damage was found in St. Louis, MO (23.0%), and water was reported to collect occasionally in the basement in approximately 40% of the homes in Watertown, MA, St. Louis, MO, and Steubenville, OH. The low reporting rate in Kingston/Harriman, TN is partly related to the fact that few homes in the sample had basements (63.3% compared with 78.4% in Topeka and 93.7% to 98.3% in the other communities).

Children living in homes with indications of dampness had consistently higher rates of respiratory symptoms than did children living in homes without these indications (table 2). City-specific unadjusted odds ratios for the association between respiratory symptoms and dampness were remarkably consistent across the six communities (table 3). Similar patterns were found with the other measures of home dampness (results not shown). These city-specific values demonstrate a strong and geographically consistent association between dampness and most childhood respiratory symptoms.

When the data were combined across cities and adjusted for other predictors of respiratory symptoms, respiratory illness and symptoms, including asthma and hay fever and other nonchest illnesses, had associations with molds varying from 1.27 to 2.12 and with dampness varying from 1.23 to 2.16 (table 4). All but one of these associations were statistically significant, although the association was weakest for asthma. Similar results were obtained for water damage and water in the basement.

To assess the effects of asthma and wheeze on the association between home dampness and other respiratory symptoms, the population was stratified into

three groups: doctor-diagnosed asthmatics, wheeze without doctor-diagnosed asthma, and children with neither wheeze nor asthma. The results for molds, expressed as prevalence ratios, are given in table 5. Prevalence ratios were used for this comparison because wide variations in prevalence in the unexposed groups made odds ratios difficult to interpret. Ratios were consistently smallest among asthmatics, but this is explained in part

by the higher reporting rates among children not exposed to dampness.

After adjusting for age, height, weight, sex, city of residence, parental education, and maternal smoking, there was no difference in level of FEV<sub>1</sub> or FVC with the presence of home dampness (table 6). There was some indication that FEF<sub>25-75</sub> was negatively related to molds.

It could be argued that the excess of persistent wheeze among children living in damp homes was due to overreporting of symptoms by parents living in those homes. If such overreporting did occur, the group of children living in damp homes and reported to be symptomatic would be a healthier group than the symptomatic children living in dry homes. To investigate this issue, we investigated the relationship between persistent wheeze and pulmonary function separately for children living in homes with and without reported molds. Persistent wheeze was associated with an 8.5% deficit in FEF<sub>25-75</sub> (95% CI, 5.6% to 11.2%) among children in homes with no molds, and a 9.2% deficit (95% CI, 5.5% to 12.7%) in homes with molds af-

TABLE 3  
CITY-SPECIFIC ODDS RATIOS FOR EFFECT OF DAMPNES ON SELECTED RESPIRATORY ILLNESS SYMPTOMS IN SIX U.S. CITIES

City	Respiratory Illness Symptom				
	Wheeze	Cough	Bronchitis	Chest Illness	Respiratory Illness before Age 2
Kingston, TN	1.51	3.72*	1.66*	1.31	1.55*
Steubenville, OH	1.48	1.42	1.40	1.78*	1.42
Watertown, MA	1.57	1.74	1.77	1.57	1.72
St. Louis, MO	1.53	1.98*	1.19	1.56	0.94
Topeka, KS	1.40	2.48*	1.09	1.86*	1.77*
Portage, WI	1.23	2.00*	0.90	1.38	1.43

\*  $p < 0.05$

TABLE 4  
ASSOCIATIONS BETWEEN HOME DAMPNES AND SYMPTOMS OF CHILDHOOD RESPIRATORY AND OTHER ILLNESS, ADJUSTED FOR AGE, SEX, CITY OF RESIDENCE, PARENTAL EDUCATION, AND MATERNAL SMOKING, IN SIX U.S. CITIES

Symptom	Estimated Odds Ratios for	
	Molds	Dampness
Wheeze	1.79 (1.44, 2.32)*	1.23 (1.10, 1.39)
Cough	2.12 (1.64, 2.73)	2.16 (1.64, 2.84)
Bronchitis	1.48 (1.17, 1.87)	1.32 (1.05, 1.67)
Chest illness	1.40 (1.11, 1.78)	1.52 (1.20, 1.93)
Lower respiratory illness	1.57 (1.31, 1.87)	1.68 (1.41, 2.01)
Respiratory illness before age 2	1.42 (1.12, 1.80)	1.40 (1.11, 1.78)
Asthma	1.27 (0.93, 1.74)	1.42 (1.04, 1.94)
Hay fever	1.57 (1.31, 1.87)	1.26 (1.06, 1.50)
Nonchest illness	1.40 (1.13, 1.74)	1.55 (1.25, 1.93)

\* 95% confidence limits in parentheses

2023379822

TABLE 5  
ASSOCIATIONS BETWEEN REPORTED MOLDS IN THE HOME AND  
RESPIRATORY SYMPTOMS IN ASTHMATICS, NONASTHMATIC  
WHEEZERS, AND NONASTHMATIC NONWHEEZERS  
IN SIX U.S. CITIES

Symptom	Estimated Prevalence Ratios for:		
	Asthmatics (n = 274)	Nonasthmatic Wheezers (n = 297)	Nonasthmatic Nonwheezers (n = 3,799)
Cough	1.50*	1.73*	1.59*
Bronchitis	0.88	1.41	1.74*
Chest illness	1.20	1.46	1.13
Lower respiratory illness	1.20	1.37*	1.39*
Respiratory illness before age 2	1.07	1.13	1.31*
Hay fever	1.04	1.46*	1.38*
Nonchest illness	0.99	1.51	1.31*

\*  $p < 0.05$ .

TABLE 6  
ASSOCIATIONS BETWEEN HOME DAMPNES VARIABLE AND PULMONARY  
FUNCTION IN CHILDREN, ADJUSTED FOR AGE, HEIGHT, WEIGHT,  
GENDER, CITY OF RESIDENCE, PARENTAL EDUCATION, AND  
MATERNAL SMOKING, IN SIX U.S. CITIES (n = 3,655)

Home Dampness Variable	Pulmonary Function Variable	Percent Difference Associated with Home Dampness*
Molds	FVC	0.44 (-0.27, 1.15) <sup>†</sup>
	FEV <sub>1</sub>	0.03 (-0.75, 0.82)
	FEF <sub>25-75</sub>	-1.62 (-3.19, -0.02)
Water damage	FVC	0.25 (-0.61, 1.12)
	FEV <sub>1</sub>	0.35 (-0.59, 1.30)
	FEF <sub>25-75</sub>	0.46 (-1.49, 2.45)
Basement water	FVC	0.16 (-0.54, 0.87)
	FEV <sub>1</sub>	-0.14 (-0.92, 0.65)
	FEF <sub>25-75</sub>	-1.14 (-2.74, 0.44)
Dampness	FVC	-0.09 (-0.75, 0.58)
	FEV <sub>1</sub>	-0.21 (-0.93, 0.52)
	FEF <sub>25-75</sub>	-1.06 (-2.55, 0.44)

\* Difference in mean pulmonary function, expressed as percentage of the grand mean, between children living in damp homes and children living in dry homes.

<sup>†</sup> 95% confidence interval.

ter adjusting for age, sex, height, city of residence, parental education, and maternal smoking. FEV<sub>1</sub> was similarly reduced in children with persistent wheeze, irrespective of exposure to molds. Thus, children reported to have persistent wheeze had similar pulmonary function deficits whether they lived in dry or in damp homes, a result not consistent with the hypothesis of overreporting.

The questionnaire data were used to investigate the association between the home dampness variables and a number of potential determinants of home dampness: the use of humidifiers or dehumidifiers, heating system, type of building, and age of building. There were more dehumidifiers in use in homes where molds and mildew were reported (42.0 versus 28.7%). Molds and mildew were reported in 34.9% of detached single family homes (which constituted 76% of the total sample), and in 17.3% of two-family

homes (with 13% the only other major category). Molds and mildew were reported in 34.8 to 43.4% of homes built between 1940 and 1969, and in 26.1 to 31.9% of homes built either before 1940 or after 1969. Water damage was reported in 22.0% of the homes built before 1930 and in 9.9% of homes built after 1979, with increasing reporting rates with increasing age of the homes in between. Water in the basement was reported in 47.8% of homes built before 1930, decreasing gradually to a reporting rate of 11.2% in homes built after 1979. No other associations emerged from this analysis.

#### Discussion

The results presented in this report suggest a consistent and strong association between reported dampness in the home and childhood respiratory symptoms. This association remained after adjust-

ment for city of residence, maternal smoking, age, sex, and parental education.

One explanation for these findings could be that people with children experiencing respiratory symptoms report dampness in their homes more readily than those whose children are not symptomatic. This seems unlikely, however, because the potential role of home dampness as a risk factor for respiratory illness has not received the public attention accorded to other risk factors such as parental smoking and the use of unvented combustion appliances.

Case studies (7, 10, 23) have documented increased mite populations and mold growth in damp homes. These organisms have, however, been associated primarily with causation and/or worsening of asthma. Interestingly, we find that reported asthma is the only respiratory symptom *not* consistently associated with dampness in the home. The symptom "persistent wheeze," which is closely associated with reported asthma in the data, is associated with dampness in the home. Also, the relationships with dampness were stronger among nonasthmatic children with or without persistent wheeze than among the asthmatic children (table 5). It could be argued that parents of children with doctor-diagnosed asthma tend to move or modify the home environment to make it as healthy as possible for their children.

The respiratory symptoms used in the analysis were strongly correlated. A child with one symptom was four times to more than ten times as likely to have one or more of the other respiratory symptoms than a child not having the index symptom. This makes it difficult to separate the associations between dampness in the home and the various respiratory symptoms. It is also possible that a relatively high percentage of children reporting symptoms other than wheeze or asthma have reactive airway disease. Hallett and Jacobs (43) reported that reactive airway disease was present in 80% of patients presenting with acute bronchitis. Molds have been associated with respiratory symptoms and diseases other than wheeze and asthma (23, 24).

A recent study in Edinburgh, Scotland found a highly elevated prevalence of respiratory symptoms among children living in damp homes (44). The prevalence of wheeze in the past year was as high as 38.1% in homes in which molds were reported to be present in the child's bedroom compared with 10.5% in homes where no molds were reported. There was no clear relationship between home

2023379823

dampness and bronchial lability; however, and this was interpreted as evidence that the association between home dampness and respiratory symptoms could be due to overreporting of symptoms (or a greater awareness of symptoms) among parents of children living in damp homes. The prevalence of wheeze was much higher in the damp homes in Edinburgh than in the damp homes in this study. In this study, the prevalence difference between homes with and without reported molds was only 6% (14.8 versus 8.9%). The mean of FEF<sub>25-75</sub> measurements was also lower among children living in damp homes, although only the association with molds was statistically significant. We also found that children with persistent wheeze had very similar deficits in FEF<sub>25-75</sub> and FEV<sub>1</sub> in dry and damp homes. Overreporting of wheeze in damp homes would have diluted the association between wheeze and pulmonary function level present.

Another interesting finding is the association between home dampness and reported illnesses other than those of the chest. Comparable associations have not been found in this population between smoking in the home and other nonchest illnesses (45). Nonchest illnesses may include various illnesses of the upper respiratory tract such as head colds, rhinitis, and sinusitis, which may be considered respiratory illnesses, and the association with dampness indicators is plausible. A recent study from the United Kingdom (46) has also suggested that home dampness is related to nonrespiratory symptoms.

These findings have implications both for further studies of indoor pollutants and for health policy. The effect of molds or dampness is comparable in size to the effect of passive smoking (44). Whether the respiratory illnesses produced by passive smoking and molds and dampness have similar long-term significance is unknown. Further investigation of childhood respiratory illnesses will require consideration of both of these variables simultaneously.

## References

- Voorhorst R, Spijksma-Boezeman MIA, Spijksma FTHM. Is a mite (*Dermatophagoides* sp.) the producer of the house-dust allergen? *Allergy Asthma* 1964; 10:329-34.
- Voorhorst R, Spijksma FTHM, Varekamp H, Leupen MJ, Lyklema AW. The house dust mite (*Dermatophagoides pteronyssinus*) and the allergens it produces. Identity with the house dust allergen. *J Allergy* 1967; 39:325-39.
- Smith JM. Clinical findings in children with allergy to the house dust mites. *Acta Allerg* 1970; 25:37-40.
- Korsgaard J. Mite asthma and residency. *Am Rev Respir Dis* 1983; 128:231-5.
- Andersen I, Korsgaard J. Asthma and the indoor environment: assessment of the health implications of high indoor air humidity. In: Berglund B, Lindvall T, Sundell J, eds. *Indoor air*. Vol. 1. Stockholm: Swedish Council for Building Research, 1984; 79-86.
- Bronswijk JEMH van. Hausstaub-Oekosystem und Hausstaub-Allergen(e). *Acta Allerg* 1972; 27: 219-28.
- Bronswijk JEMH van. *Dermatophagoides pteronyssinus* (Trouessart, 1897) in mattress and floor dust in a temperate climate (Acari: Pyroglyphidae). *J Med Entomol* 1973; 10:63-70.
- Murray AB, Zuk P. The seasonal variation in a population of house dust mites in a North American city. *J Allergy Clin Immunol* 1979; 64:266-9.
- Arlian LG, Bernstein IL, Gallagher JS. The prevalence of house dust mites, *Dermatophagoides* spp, and associated environmental conditions in homes in Ohio. *J Allergy Clin Immunol* 1982; 69: 527-32.
- Korsgaard J. House dust mites and absolute indoor humidity. *Allergy* 1983; 38:85-92.
- Berrens L, Young E, Zuidema P. A comparative chemical and clinical investigation of house dust extracts from alpine and lowland regions. *Acta Allerg* 1971; 26:200-12.
- Vervloet D, Penaud A, Razzouk H, et al. Altitude and house dust mites. *J Allergy Clin Immunol* 1982; 69:290-6.
- Voorhorst R. Quantitative aspects of the problem of house dust atopy and house dust mites. *Acta Allerg* 1970; 25:237-54.
- Sørensen H, Gravesen S, Lind P, Schwartz B, Ashoor AA, Maglad S. The occurrence of indoor allergens in Saudi Arabia. *Ann Allergy* 1985; 54: 530-31.
- Murray AB, Ferguson AC, Morrison BJ. Sensitization to *Dermatophagoides farinae* (Df) and *D. pteronyssinus* (Dp) in different climatic areas (abstract). *J Allergy Clin Immunol* 1984; 73:158.
- Storm van Leeuwen W, Varekamp H, Bien L. Asthma bronchiale und Klima. *Klin Wochenschr* 1924; 3:520-3.
- Dowse GK, Turner KJ, Stewart GA, Alpers MP, Woolcock AJ. The association between *Dermatophagoides* mites and the increasing prevalence of asthma in village communities within the Papua New Guinea highland. *J Allergy Clin Immunol* 1985; 75:75-83.
- Gravesen S. Fungi as a cause of allergic disease. *Allergy* 1979; 34:134-54.
- Salvaggio J, Aukrust L. Mold induced asthma. *J Allergy Clin Immunol* 1981; 68:327-46.
- Holmberg K. Moulds as an agent in respiratory symptoms. In: Berglund B, Lindvall T, Sundell J, eds. *Indoor air*. Vol. 3. Stockholm: Swedish Council for Building Research, 1984:233-8.
- Reed CE. What we do and do not know about mould allergy and asthma. *J Allergy Clin Immunol* 1985; 76:773-5.
- Solomon WR. Fungus aerosols arising from cold mist vaporizers. *J Allergy* 1974; 54:222-8.
- Kozak PP, Gallup J, Cummins LH, Gillman SA. Currently available methods for home mould surveys II. Examples of problem homes studied. *Ann Allergy* 1980; 45:167-75.
- Fergusson RJ, Milne LJR, Crompton GK. Penicillium allergic alveolitis: faulty installation of central heating. *Thorax* 1984; 39:294-8.
- Richards M. Atmospheric mould spores in and out of doors. *J Allergy* 1954; 25:429-39.
- Gravesen S. Identification and quantitation of indoor airborne microfungi during 12 months from 44 Danish homes. *Acta Allerg* 1972; 27:337-54.
- Hirsch SR, Sosman JA. A one-year survey of mould growth inside 12 homes. *Ann Allergy* 1976; 36:30-8.
- Solomon WR. A volumetric study of winter fungi prevalence in the air of mid-western homes. *J Allergy Clin Immunol* 1976; 57:46-55.
- Kozak PP, Gallup J, Cummins LH, Gillman SA. Factors of importance in determining the prevalence of indoor moulds. *Ann Allergy* 1979; 43: 88-94.
- Calvo MA, Guarro J, Suarez G, Ramirez C. Airborne fungi in the air of Barcelona, Spain IV. Studies of the spore content of air in dwellings. *Ann Allergy* 1980; 44:228-34.
- Beaumont F, Kauffman HF, Sluiter HJ, Vries K de. A volumetric-aerobiologic study of seasonal fungi prevalence inside and outside dwellings of asthmatic patients living in northeast Netherlands. *Ann Allergy* 1984; 53:486-92.
- Gravesen S. Indoor airborne mould spores. *Allergy* 1985; 40(Suppl 3:21-3).
- Melia RJW, Florey Cdu V, Morris RW, Goldstein B, John H, Clark C, Craighead I, Mackinlay J. Childhood respiratory illness and the home environment II. Association between respiratory illness and nitrogen dioxide, temperature and relative humidity. *Int J Epidemiol* 1982; 11:164-9.
- Lesourd BM, Corriel RN, McBryde JL, Kniker WT. Cell mediated immunity in school children assessed by multitest CMI skin testing II. Epidemiologic factors affecting immune responsiveness. *Ann Allergy* 1985; 54:446-52.
- Varekamp H, Voorhorst R. De invloed van klimaat en behuizing op patiënten met asthma bronchiale en rhinitis vasomotoria. *Ned Tijdschr Geneesk* 1961; 105:2022-8.
- Leupen MJ. Discussion. In: Fanger PO, Valbjørn O, eds. *Copenhagen: Indoor Climate Danish Building Research Institute*, 1979:124-5.
- Ferris BG Jr. Project Coordinator. Epidemiology Standardization Project. *Am Rev Respir Dis* 1978; 118(Part 2:1-120).
- Ware JH, Dockery DW, Spiro A III, Speizer FE, Ferris BG Jr. Passive smoking, gas cooking, and respiratory health of children living in six cities. *Am Rev Respir Dis* 1984; 129:366-74.
- Tobin RS, Baranowski E, Gilman AP, Kuiper-Goodman T, Miller JD, Giddings M. Significance of fungi in indoor air: report from a working group. *Can J Public Health* 1987; 78:S1-S32.
- Dockery DW, Berkey CS, Ware JH, Speizer FE, Ferris BG Jr. Distribution of FVC and FEV<sub>1</sub> in children 6 to 11 years of age. *Am Rev Respir Dis* 1983; 128:405-12.
- Spengler JD, Ware J, Speizer F, et al. Harvard's indoor air quality respiratory health study. Proceedings of the 4th International Conference on Indoor Air Quality and Climate, Institute for Water, Soil and Air Hygiene, Berlin, GDR, 1987; 2:218-23.
- SAS Institute Inc. SAS User's Guide: Statistics. Version 5. Cary, N.C.: SAS Institute, 1985:956.
- Hallett JS, Jacobs RL. Recurrent acute bronchitis: the association with undiagnosed bronchial asthma (abstract). *J Allergy Clin Immunol* 1983; 71:97.
- Strachan DP. Damp housing and childhood asthma: validation of reporting of symptoms. *Br Med J* 1988; 297:1223-6.
- Dockery DW, Spengler JD, Speizer FE, Ferris BG Jr, Ware JH, Brunekreef B. Associations of health status with indicators of indoor air pollution from an epidemiologic study in six U.S. cities. Proceedings of the 4th International Conference on Indoor Air Quality and Climate, Berlin, GDR, 1987; 2:203-7.
- Martin CJ, Platt SD, Hunt SM. Housing conditions and ill health. *Br Med J* 1987; 294:1125-7.



2023379825

Berwick, M., Leaderer, B.P., Stolwijk, J.A. "Lower Respiratory Symptoms in Children Exposed to Nitrogen Dioxide from Unvented Combustion Sources" Environment International 15: 369-373, 1989.

SUMMARY: A prospective epidemiologic study was carried out for 12 weeks in the winter of 1983 to evaluate the impact of indoor air contaminant levels on respiratory health. A group of 121 children below the age of 13 (59 with unvented kerosene space heaters in the home; 62 without) were enrolled in the study and nitrogen dioxide levels were measured in 93% of the subjects' homes for one two-week period. When socioeconomic status and history of respiratory illness were controlled, children under the age of seven exposed to 30 ug/m<sup>3</sup> or more of nitrogen dioxide were found to have a risk of reporting lower respiratory symptoms 2.25 times (95% C.I. 1.69-4.79) that of children who were not exposed. Aspects of our study design, including increased precision of exposure classification and the inclusion of very young children, may explain our findings.

2023379826

## LOWER RESPIRATORY SYMPTOMS IN CHILDREN EXPOSED TO NITROGEN DIOXIDE FROM UNVENTED COMBUSTION SOURCES

Marianne Berwick, Brian P. Leaderer, and J.A. Stolwijk  
J.B. Pierce Foundation and Yale University, New Haven, CT 06510, USA

Rebecca T. Zgraniskii  
Center for Disease Control, Atlanta, GA, USA

*EI 87-371 (Received 10 November 1987; Accepted 3 April 1989)*

A prospective epidemiologic study was carried out for 12 weeks in the winter of 1983 to evaluate the impact of indoor air contaminant levels on respiratory health. A group of 121 children below the age of 13 (59 with unvented kerosene space heaters in the home; 62 without) were enrolled in the study and nitrogen dioxide levels were measured in 93% of the subjects' homes for one two-week period. When socioeconomic status and history of respiratory illness were controlled, children under the age of seven exposed to 30  $\mu\text{g}/\text{m}^3$  or more of nitrogen dioxide were found to have a risk of reporting lower respiratory symptoms 2.25 times (95% C.I. 1.69-4.79) that of children who were not exposed. Aspects of our study design, including increased precision of exposure classification and the inclusion of very young children, may explain our findings.

### INTRODUCTION

Conflicting evidence exists for a relationship between low levels of nitrogen dioxide, such as those that commonly occur in homes with unvented combustion sources, and adverse health effects, such as increased respiratory illness (Keller et al. 1979; Lebowitz et al. 1983; Melia et al. 1977, 1979, 1982; Speizer et al. 1980; Ware et al. 1984). Much of the research has been constrained to measure exposure by proxy—the presence or absence of a source, usually a gas cooking stove. While obtaining environmental measurements of exposure has been difficult due to expense and the greater level of cooperation entailed by respondents, the assumption has not been justified that the presence or absence of an unvented gas appliance is sufficient to categorize

the exposure of a population. Nitrogen dioxide ( $\text{NO}_2$ ) levels in homes using electricity for cooking have been measured at levels as high as 33.8  $\mu\text{g}/\text{m}^3$  (Goldstein et al. 1979). A number of factors, such as ventilation rate and the presence of other unnoted unvented combustion appliances, are frequently difficult to measure and can cause this wide range in exposure levels.

To assess the existence and the magnitude of an association between  $\text{NO}_2$  levels and adverse respiratory outcomes, we wanted to capitalize on the increased use of kerosene heaters and their potentially high  $\text{NO}_2$  emissions. Because  $\text{NO}_2$  has been hypothesized to interfere with host defense mechanisms, lower respiratory illness, represented by symptom reports, was used to examine the association between

NO<sub>2</sub> and adverse health outcomes. Since acute respiratory infections are frequent, particularly among young children, greater power to detect differences in illness rates could be obtained from observing a relatively small number of subjects. In addition, reports in the literature indicated that young children would be most likely to be sensitive to any adverse effects from NO<sub>2</sub>.

## METHODS

### *Study design*

A prospective cohort study of adult women and children was conducted from January to April 1983 in New Haven, CT, to delineate associations between low levels of indoor air contaminant levels (including NO<sub>2</sub>, sulphur dioxide, and formaldehyde) and respiratory symptoms. A group of 121 children under the age of 13 was enrolled in this study, 59 living in homes with kerosene space heaters and 62 living in homes without heaters. To study the association between low levels of NO<sub>2</sub> and respiratory symptoms, we systematically chose one child from each family under the age of 13 and closest in age to 5. The participation rate was 78% of families living in homes with kerosene heaters, and 81% of those living in homes without heaters. The air monitoring design is described elsewhere (Leaderer et al. 1986).

### *Data collection*

Data were gathered from several sources: baseline in-person interviews, 6 follow-up telephone interviews, measurements from passive monitors placed in 93% of the homes, and town tax assessor record abstracts.

The baseline interviews were administered between October 1, 1982, and January 14, 1983, and gathered information on demographics, medical history, building characteristics, and homeowner's heating patterns.

Follow-up telephone interviews were administered bi-weekly from January 30, 1983, to April 2, 1983. These consisted of: (1) a symptom checklist covering 20 symptoms of upper respiratory illness, lower respiratory illness, symptoms of general malaise, and a count of the number of days with each symptom, and (2) current heating patterns.

Data abstracted from town tax assessor records included the assessed value of the home, the materials used, the condition of the home, its age, the type of heating system and fuel used, the number of rooms and floors in the home, and the square footage of the bottom floor.

Approximately 93% of the children's homes were monitored with passive diffusion tubes for NO<sub>2</sub> for at least one two-week period. These tubes were placed in three locations inside the residence and one location outside. Sulphur dioxide, formaldehyde, and air infiltration rates were measured in a subsample of homes, but will not be reported here.

### *Definition of respiratory illness*

The outcome variable of interest in this study was maternally reported acute respiratory illness, particularly lower respiratory illness. Lower respiratory symptoms included: fever, chest pain, productive cough, wheeze, chest cold, physician-diagnosed bronchitis, physician-diagnosed pneumonia, and asthma. Upper respiratory symptoms were also ascertained. They included: fever, sore throat, nasal congestion, dry cough, croup, and head cold. As the data were too sparse to analyze by individual symptom, clusters of lower respiratory symptoms and upper respiratory symptoms were formed, and incidence was summed for the entire study period of 12 weeks. A symptom cluster was considered present if two or more symptoms in the cluster were reported for one time period.

### *Definition of exposure*

Accurate classification of subjects by exposure to NO<sub>2</sub> was a major priority of this project. During the study, exposure definition was improved beyond the anticipated dichotomy, so that children, who were initially identified as exposed or unexposed as a function of living in a home with a kerosene space heater or not, were classified according to measured NO<sub>2</sub> levels. Since measurements were taken for only one two-week period, NO<sub>2</sub> levels were estimated for all other periods based on hours of use multiplied by the level of NO<sub>2</sub> estimated during burning. These estimates were not significantly different from the measured NO<sub>2</sub> levels which were determined to be the least biased indicator of household exposure to NO<sub>2</sub> and thus were chosen as the most refined exposure variable.

Personal exposure estimates indicated a 94% correlation ( $p < 0.01$ ) between monitors worn by a subsample of 23 adult subjects and the average estimate of the three monitored rooms in the household during the same time period. No higher correlation has appeared in the literature, and, in fact, Remijn (1985) reported that the household average NO<sub>2</sub> measurement is an excellent proxy for personal exposures.

2023379828

### Data analysis

Data were edited for consistency, coded, and quality control measures undertaken as the data were entered. Unconditional logistic regression analyses were performed to determine the magnitude and statistical significance of each factor controlling for all other variables in the model. With the exception of age, all the independent variables were continuous. Age was treated as dichotomous—younger than seven years and seven years and older. It should be emphasized that this type of analysis allows only a general comparison of variables and is highly dependent on the choice of cutpoint. Adjusted odds ratios were calculated using the LOGIST procedure of the Statistical Analysis System (Harrell 1983). Similar techniques were also used to assess effect modification and statistical interaction.

## RESULTS

### Demographic characteristics

Comparisons were made among the 113 monitored children as well as the 8 who were not monitored. They were very similar. The mean age of the children was 6.7 years, and 82% were away from home approximately 6 hours per day in school or daycare. The average household size was 4.2, the average socioeconomic status was moderate (Hollingshead 4-fac-

tor index)—42.5, and all children were Caucasian. There were approximately equal numbers of boys and girls in each group.

### Measured household exposures to NO<sub>2</sub>

Table 1 shows the measured NO<sub>2</sub> levels by each major category of NO<sub>2</sub> source: Kerosene Heater, Gas Stove, Gas Stove plus Kerosene Heater, and No Source.

### Health effects: Lower respiratory symptoms

To assess the effect of NO<sub>2</sub> levels on the presence or absence of lower respiratory symptoms, while simultaneously controlling for effect modifiers and potential confounders, multiple logistic regression was carried out for the binary dependent variable, presence or absence of lower respiratory symptoms. Independent variables were included that had statistically significant relationships with respiratory symptoms in this study (SES, history of respiratory illness), and those which were cited in other studies as being important (household size, age, number of cigarettes smoked in the house per day, and exposure to NO<sub>2</sub>).

Children under the age of 7 who were exposed to 30 µg/m<sup>3</sup> NO<sub>2</sub> had an odds for being reported as having lower respiratory symptoms 2.25 (95% C.I. 1.69-4.79) times those of unexposed children the

Table 1. Measured NO<sub>2</sub> values (µg/m<sup>3</sup>) in homes of monitored children (n=113) by source presence, Yale Health and Heating Study, New Haven, CT, area, winter 1983.

	Kerosene Heater + Gas Stove n=6	Kerosene Heater Only n=49	Gas Stove Only n=13	No Source n=4
Kitchen	89.50	41.07	40.92	6.40
Living Room	76.00	43.40	24.85	6.23
Bedroom	104.75	38.33	28.54	5.19
House Average	90.08	40.93	31.43	5.94

2023379829

Table 2. Association between measured NO<sub>2</sub> levels and reported lower respiratory symptoms, by multiple logistic regression analysis, in 113 monitored children in the Yale Health and Heating study, New Haven, CT, area, winter 1983.

Variable	Odds ratio	95% CI
Age	1.05	0.91-1.21
SES**	2.35	1.14-4.85
History of		
Respiratory Illness	1.29	1.03-1.62
Age < 7 *30 µg/m <sup>3</sup> NO <sub>2</sub>	2.25	1.69-4.79
Age ≥ 7 *30 µg/m <sup>3</sup> NO <sub>2</sub>	0.84	0.59-1.42

\*Hosmer goodness-of-fit:  $\chi^2 = 6.41$ , 6 d.f.,  $p=0.38$ .

\*\*20 units on the Hollingshead scale.

same age when the effects of a history of respiratory illness and SES were controlled (Table 2).

NO<sub>2</sub> exposure appeared to have no effect on reported lower respiratory symptoms in children aged seven or older. A history of respiratory illness and socioeconomic status contributed significantly and independently to the risk for reported lower respiratory symptoms. Children of higher socioeconomic status (20 units on the Hollingshead scale) were 2.4 times as likely as children of lower SES to be reported as having lower respiratory symptoms. A history of respiratory illnesses made the odds of reporting lower respiratory symptoms 1.3 times as likely in all the children. Exposure to environmental tobacco smoke was not significantly associated with reported symptoms in either age group.

#### DISCUSSION

In this study the ability to measure acute effects at the same time as exposure seems to have allowed for more precise estimates of the associated health effects—in terms of lower respiratory symptoms, the range of the susceptible group (less than seven years old), and other potentially important risk factors. Since the previous literature has shown inconsistent results, it seems that the effect of NO<sub>2</sub> is likely to be limited in many regards. It is plausible that there is a real biological effect, based on animal data and the trend toward seeing an effect in younger ages. Many

studies have reported that SES plays a significant role as does a history of previous respiratory illness (see e.g., Monto and Ullman 1974).

A major strength of this study was that misclassification of exposure was limited, though not entirely, by the individual household measurement of NO<sub>2</sub> levels during one two-week period. If this study used dichotomous source classification (i.e., presence or absence of an unvented combustion source), as most research has been constrained to do, the association between lower respiratory symptoms and exposure would have been only marginally significant ( $p=0.08$ ). Thus, the qualitative nature of previous data may have obscured the ability to define association between NO<sub>2</sub> and respiratory effects.

A limitation to the findings from this study is the currently unknown bias inherent in maternal reports of symptoms. However, we found no association between a mother's initial report of her child's propensity to illness assessed at baseline and subsequent reports of symptoms throughout the study.

#### CONCLUSION

The study has demonstrated a statistically significant association between NO<sub>2</sub> concentrations and the incidence of two or more lower respiratory symptoms in children under seven years of age. No such association was seen in older children. A history of previous respiratory illness and socioeconomic status

2023379830

were significantly and independently associated with reported illness. This research has important implications for the present and possibly future health of young children exposed to  $\text{NO}_2$  from any unvented combustion. The conclusions, however, are limited to this population and must be replicated, possibly with a population exposed to higher levels of  $\text{NO}_2$ , before they can be relied on as a basis for further action.

**Acknowledgment** — This investigation received support from Grant No. ES-00354 from N.I.E.H.S., Contract No. CPSC-P-83-1196 from the Consumer Product Safety Commission, The J.B. Pierce Foundation, A Small Grant from Sigma Xi, and Grant No. ES-07087-05 from N.I.E.H.S.

## REFERENCES

- Goldstein, B. D.; Melia, R. J. W.; Chinn, S.; Florey, C. V.; Clark, D.; John, H. H. The relation between respiratory illness in primary school children and the use of gas for cooking. II. Factors affecting nitrogen dioxide levels in the home. *Int. J. Epidemiol.* 8:339-345; 1979.
- Harrell, F. The logist procedure. Cary, NC: Sas Supplemental Library User's Guide; 1983.
- Keller, M. D.; Lanese, R. R.; Mitchell, R. J.; Cole, R. W. Respiratory illness in households using gas and electricity for cooking. II. Symptoms and objective findings. *Environ. Res.* 11:504-515; 1979.
- Leaderer, B. P.; Zgraniski, R. T.; Berwick, M.; Stolwijk, J. A. J. Assessment of exposure to indoor air contaminants from combustion sources: methodology and application. *Amer. J. Epidemiol.* 124:275-289; 1986.
- Lebowitz, M. D.; Holberg, C. J.; O'Rourke, M. K.; Gorman, G.; Dodge, R. Gas stove usage, CO and TSP, and respiratory effects. Proceedings of the 76th annual meeting of the Air Pollution Control Association. Available from: APCA Pittsburgh, PA; 1983.
- Melia, R. J. W.; Florey, C. V.; Altman, D. G.; Swan, A. V. Association between gas cooking and respiratory disease in children. *Br. Med. J.* 2:149-152; 1977.
- Melia, R. J. W.; Florey, C. V.; Chinn, S. The relation between respiratory illness in primary school children and the use of gas for cooking. I. Results from a national survey. *Int. J. Epidemiol.* 8:333-338; 1979.
- Melia, R. J. W.; Florey, C. V.; Morris, R. W.; Goldstein, B. D.; John, H. H.; Clark, D.; Craighead, I. B.; McKinlay, J. C. Childhood respiratory illness and the home environment. II. Association between respiratory illness and nitrogen dioxide, temperature, and relative humidity. *Int. J. Epidemiol.* 11:164-169; 1982.
- Monto, A. S.; Ullman, B. M. Acute respiratory illness in an American community: the Tecumseh study. *J. Am. Med. Assoc.* 227(2):164-169; 1974.
- Remijn, B.; Fisher, P.; Brunekreef, B.; Lebret, E.; Boeleij, J. S. M.; Noij, D. Indoor air pollution and its effect on pulmonary function of adult non-smoking women. I. Exposure estimates for nitrogen dioxide and passive smoking. *Int. J. Epidemiol.* 14:219-224; 1985.
- Speizer, F. E.; Ferris, B.; Bishop, Y. M. M.; Spengler, J. Respiratory disease rates and pulmonary function in children associated with  $\text{NO}_2$  exposure. *Am. Rev. Respir. Dis.* 121:3-10; 1980.
- Ware, J. H.; Dockery, D. W.; Spiro, A.; Speizer, F. E.; Ferris, Jr., B. G. Passive smoking, gas cooking, and respiratory health of children living in six cities. *Am. Rev. Respir. Dis.* 129:366-374; 1984.

2023379831

30

2023379832



Hurwitz, E.S., Gunn, W.J., Pinsky, P.F., Schonberger, L.B. "Risk of Respiratory Illness Associated with Day-care Attendance: A Nationwide Study" Pediatrics 87(1): 62-69, 1991.

**ABSTRACT.** The risk of respiratory and other illnesses in children (age groups: 6 weeks through 17 months, 18 through 35 months, and 36 through 59 months) in various types of day-care facilities was studied. Children considered exposed to day care were those who were enrolled in day care with at least one unrelated child for at least 10 hours per week in each of the 4 weeks before the interview; unexposed children were not enrolled in any regular child care with unrelated children and did not have siblings younger than 5 years of age receiving regular care with unrelated children. Although an increased risk of respiratory illness was associated with attending day care for children in all three age groups, this risk was statistically significant only for children 6 weeks through 17 months of age (odds ratio = 1.6; 95% confidence interval = 1.1 to 2.4) and children 18 through 35 months of age who had no older siblings (odds ratio = 3.4; 95% confidence interval = 2.0 to 6.0). In contrast, day-care attendance was not associated with an increased risk of respiratory illness in children 18 through 35 months of age with older siblings (odds ratio = 1.0). For children aged 6 weeks through 17 months, the exposure to older siblings was associated with an increased risk of respiratory illness; however, for children aged 36 through 59 months, older siblings were protective against respiratory illness. In addition, for the children in each age group currently in day care, increased duration of past exposure to day care was associated with a decreased risk of respiratory illness. It is estimated that during the period of the study approximately 10% of respiratory illnesses in the United States in children younger than 5 years of age were attributable to day-care attendance.

2023379833

# Risk of Respiratory Illness Associated with Day-care Attendance: A Nationwide Study

Eugene S. Hurwitz, MD; Walter J. Gunn, PhD; Paul F. Pinsky, MPH;  
and Lawrence B. Schonberger, MD

From the Division of Viral and Rickettsial Diseases, Center for Infectious Diseases, Center for Disease Control, Public Health Service, US Department of Health and Human Services, Atlanta, Georgia

**ABSTRACT.** The risk of respiratory and other illnesses in children (age groups: 6 weeks through 17 months, 18 through 35 months, and 36 through 59 months) in various types of day-care facilities was studied. Children considered exposed to day care were those who were enrolled in day care with at least one unrelated child for at least 10 hours per week in each of the 4 weeks before the interview; unexposed children were not enrolled in any regular child care with unrelated children and did not have siblings younger than 5 years of age receiving regular care with unrelated children. Although an increased risk of respiratory illness was associated with attending day care for children in all three age groups, this risk was statistically significant only for children 6 weeks through 17 months of age (odds ratio = 1.6; 95% confidence interval = 1.1 to 2.4) and children 18 through 35 months of age who had no older siblings (odds ratio = 3.4; 95% confidence interval = 2.0 to 6.0). In contrast, day-care attendance was not associated with an increased risk of respiratory illness in children 18 through 35 months of age with older siblings (odds ratio = 1.0). For children aged 6 weeks through 17 months, the exposure to older siblings was associated with an increased risk of respiratory illness; however, for children aged 36 through 59 months, older siblings were protective against respiratory illness. In addition, for the children in each age group currently in day care, increased duration of past exposure to day care was associated with a decreased risk of respiratory illness. It is estimated that during the period of the study approximately 10% of respiratory illnesses in the United States in children younger than 5 years of age were attributable to day-care attendance. *Pediatrics* 1991; 87:62-69; day-care facilities, respiratory illness.

**ABBREVIATIONS.** ARE, attributable risk in the exposed; PAR, population attributable risk; CI, confidence interval.

In recent years, interest has been growing in the possible health-related risks that result from the increasing use of day-care facilities in the United States. Among the illnesses of concern are infections of the upper respiratory tract, the most common cause of illness in children attending day-care facilities, as well as diarrheal illnesses, hepatitis, and *Haemophilus influenzae* infections. Infections of the upper respiratory tract, although typically mild, are of increasing interest because of their possible association with otitis media and associated complications.<sup>1,2</sup> We conducted a study to assess the risk of respiratory and other illness related to attending various types of day-care facilities. This study provided the opportunity to assess the risk of respiratory illness in children of various ages attending day-care facilities and to assess previously suggested characteristics of day-care exposure and their potential role in the risk of day-care-associated respiratory illnesses.

## METHODS

The study was designed to compare the rates of respiratory and other illnesses in exposed vs unexposed cohorts of children in each of three age groups: 6 weeks through 17 months (group 1), 18 through 35 months (group 2), and 36 through 59 months (group 3). Exposed children were defined as having child care with at least one unrelated child for at least 10 hours per week in each of the 4 weeks before interview. A child was considered unexposed if neither the child nor any siblings

Received for publication Aug 21, 1989; accepted Jan 30, 1990.  
Reprint requests to (L.B.S.) Mail Stop A-32, Division of Viral and Rickettsial Diseases, Center for Infectious Diseases, Centers for Disease Control, Public Health Service, US Dept of Health and Human Services, Atlanta, GA 30333.  
PEDIATRICS (ISSN 0031-4005). Copyright © 1991 by the American Academy of Pediatrics.

younger than 5 years of age had any regular child care with unrelated children during this interval. The study was designed to enroll at least 262 exposed and 262 unexposed children from each age group.

Children in the study cohorts were selected through a nationwide telephone survey that incorporated a random digit-dialing, cluster-sampling technique. A preliminary screener determined the age and exposure status of any children younger than 5 years of age in the household. The parents of all exposed children and a random sample of unexposed children (who were relatively more prevalent than exposed children) were subsequently administered an in-depth questionnaire which sought information including the occurrence of any respiratory or diarrheal illnesses and associated symptoms in children in the previous 2 weeks; exposure (both in and outside the home) to other children, immunization histories, and current and past child-care arrangements.

All interviews were conducted between March 12 and June 17, 1987. More than 35 000 households were called; 28 500 (81%) agreed to participate by completing the screening and when selected, the in-depth questionnaire. Of the participating households, 10% (2853) had children younger than 5 years of age. Of the 3475 children identified in these households, 29% could be classified as exposed, 60% as unexposed, and 11% did not meet the study definition of exposed or unexposed.

### Analyses

Primary analyses in this study focused on comparing the risk of respiratory illness among exposed and unexposed cohorts within 2 weeks before the interview; analyses were conducted separately for each age group. Although multiple children from the same household were enrolled in this study, one child at most (the youngest) from a given household was included in the analysis of each age group. This ensured that all the observations within each age group were independent; hence, standard statistical techniques could be used in each separate analysis. Comparisons of risk between age groups were conducted restricting the analysis to children without siblings.

To control for the effect of possible confounders and to identify potential interaction effects, we used multiple logistic regression analysis. Logistic models were developed as follows. For each age group, factors previously reported or suspected of being risk factors for childhood illnesses were screened by using Mantel-Haenszel statistics (see Table 1). The factors identified as potential con-

TABLE 1. Variables Considered for Multivariate Models

Region of country
Race (white, nonwhite)*
Income (<\$20 000)*
Mother's education (<high school)
Crowding (1 or more persons per room)
Work in day care or babysitting
Smoking at home by family members*
Siblings in household*
Current breast-feeding (age group 1 only)*
Month of interview*

\* Core variables selected for inclusion in model. (The variables without asterisks were not included in the model because eliminating them changed the exposure odds ratio by less than 5%.)

founders or interaction variables in any age group were selected as core variables, which were used in the logistic models for each of the three age groups. The variable "current breast-feeding" was used only in the youngest age group.

Logistic regression analyses were completed separately for each age group. The baseline logistic model included exposure, age, and the core variables as main effects. Two-way interaction terms involving exposure were then added to the baseline model stepwise (*P* value to enter, .05). Finally, the variables not involved in significant interactions were dropped from the model if their absence changed the exposure odds ratio by less than 5%.

We also examined the following three characteristics of day-care exposure to assess their association with respiratory illness: number of other children in the day-care setting, number of hours per week currently in day care, and length of time previously in day care. To simplify the analysis of these factors, we eliminated from the exposed group the children who were currently attending more than one day-care facility or who had switched day-care facilities. Multivariate logistic models incorporating these additional variables were developed from the final exposure models already described.

To take into account the complex survey design, we used RtiLogit, a program that incorporates the design effect into the variance estimates of the logistic parameters, to run the final logistic models.

### Illness in Families

The rates of respiratory illness in the families of exposed children and the families of unexposed children were also examined. Families were classified as exposed if a child (in any age group) attended day care; they were classified as unexposed if their children did not attend day care. Again, multivariate models were developed, as described earlier.

TABLE 2. Demographic Characteristics of Children Exposed (Exp) and Children Unexposed (Unexp) to Day Care by Age Group

Characteristic	Age Group					
	6 wk-17 mo		18-35 mo		36-59 mo	
	Exp (n = 192)	Unexp (n = 351)	Exp (n = 302)	Unexp (n = 383)	Exp (n = 463)	Unexp (n = 446)
Mean age, mo	11.0	9.0	27.0	26.8	48.4	47.1
Race/ethnicity, %						
White	77.2	74.6	82.2	76.5	72.3	73.3
Black	7.8	8.3	9.6	9.1	14.6	9.0
Hispanic	6.2	11.7	2.6	7.6	6.0	9.9
Other/unknown	8.8	5.4	5.6	6.8	7.1	7.8
Maternal education, %						
<High school	6.4	14.6	7.1	13.7	6.7	10.9
High school	42.3	43.9	40.2	43.3	39.2	52.4
Some college	24.3	24.5	26.0	22.5	26.2	21.4
College degree	27.0	17.0	26.7	20.5	28.0	15.3
Income (in thousands), %						
<\$20	24.4	34.8	23.1	32.1	23.2	35.7
\$20-35	32.6	33.6	33.3	36.6	30.1	34.8
>\$35	38.9	25.6	38.6	26.1	40.6	22.4
Unknown	4.2	6.0	5.0	5.2	6.0	7.2
Region, %						
Northeast	16.6	25.9	19.8	26.9	19.6	19.5
South	37.8	23.1	34.0	25.9	36.8	24.9
North Central	25.9	28.5	26.1	25.3	26.2	30.5
West	19.7	22.5	20.1	21.9	17.4	25.1
Siblings <18, %						
None	39.6	27.9	40.7	23.0	25.9	13.5
Older	60.4	72.1	52.0	64.5	55.3	64.3
Younger only	0	0	7.3	12.5	18.8	22.2

### Attributable Risk

The attributable risk in the exposed (ARE) estimates the percentage of cases of illness in exposed children that is attributable to the exposure (day care); the population attributable risk (PAR) measures the percentage of the total cases of illness in exposed children and unexposed children that is attributable to the exposure.

For each age group the ARE and the PAR were calculated by using the following formulas:

$$ARE = (I_E - I_U)/I_E$$

$$PAR = P_E (I_E - I_U)/I$$

where  $I$  is the 2-week age-specific incidence of respiratory illness in the total population and  $P_E$  is the proportion of the total population exposed to day care. Because this study excluded children exposed 1 to 10 hours per week, we assumed in estimating  $I$  that the incidence in this group was similar to the incidence in the unexposed group.  $I_E$  represents the estimated incidence of respiratory illness in the exposed population;  $I_U$  is the estimated incidence in a demographically similar unexposed population (ie, adjusted for income, race, and presence of siblings). Logistic regression models were used to calculate these incidence rates.

### Selected Infectious Diseases in Past Year

Included in the questionnaire were questions about the occurrence in the past year of overnight hospitalizations and 15 specific infectious diseases. Because the exposures and the ages of subjects were different, these analyses were done on a person-year basis. Rates were standardized for region, income, and presence of siblings. Statistical significance was assessed by using the method of Breslow and Day to compare standardized mortality ratios.

### RESULTS

#### Demographic Characteristics

Comparing the demographic characteristics of the exposed and the unexposed cohorts in each age group revealed that the unexposed tended to have lower levels of maternal education and household income and were more likely to be of Hispanic ancestry (Table 2). Unexposed children were also more likely to have siblings than were exposed children and less likely to live in the South. These and other differences between exposed and unexposed cohorts were considered and, where appropriate, adjusted for in subsequent multiple logistic analyses.

### Characteristics of Day-care Exposure

Table 3 displays various characteristics of day-care exposure. As required by the definition of day-care exposure, all children were enrolled for at least 10 hours per week. Approximately 50% of children in each age group were in day care for 40 or more hours per week (mean time in each age group: 35, 34, and 33 hours per week, respectively). Prior time in day care increased as age increased; almost half (47%) of the children in group 3 had been enrolled in day care for at least 18 months. The percentage of exposed children in small child-care arrangements (6 or fewer children) decreased with age, ranging from 70% of children in group 1 to only 31% of children in group 3.

### Antecedent Illnesses and Events

During the 2 weeks before the interview, the children in all three age groups exposed to day care were more likely to have had a respiratory illness than those not exposed to day care. Furthermore, in each group of children with a respiratory illness, a higher percentage of exposed than unexposed children reported two or more respiratory symptoms (ie, cough, fever, runny nose, sore throat, earache), received antibiotics, and consulted or visited a health care provider (Table 4).

Multiple logistic regression analyses demonstrated that the overall odds ratio for respiratory illness associated with day-care exposure was 1.6 (95% confidence interval [CI], 1.1 to 2.4) for children in group 1 and 1.3 (95% CI, 0.95 to 1.8) for children in group 3 (Table 5). Among those in group 2, the presence of siblings significantly reduced the odds ratio for day-care exposure. Further analysis in this age group of the effect of siblings demonstrated that the day-care odds ratio for children

with younger siblings only was similar to that for children with no siblings and that the aggregate odds ratio for these children was significantly elevated (3.4, 95% CI, 2.0 to 6.0). In contrast, the odds ratio for children with older siblings was significantly lower than above and not significantly different from 1. In the other age groups the odds ratio was not significantly affected by the presence of siblings.

Multiple logistic analysis concerning children without siblings (thereby allowing direct comparisons of age groups) demonstrated day-care odds ratios of 1.8, 3.7, and 1.5 for age groups 1, 2, and 3, respectively. The odds ratio for children in group 2 was 2.0-fold higher (95% CI, 0.74 to 5.4) than that for children in group 1 and 2.4-fold higher (95% CI, 0.93 to 6.4) than that for children in group 3.

To further assess the possible independent risk of respiratory illness due to exposure to older siblings, we also calculated odds ratios of respiratory illness associated with other siblings (Table 5). In group 1, the odds ratio (1.7) was significantly elevated. In group 3, the odds ratio was significantly below 1, suggesting that in this age group the risk of respiratory illness was lower in children with older siblings than in those without. In both these groups, no interaction with day-care exposure was observed. For children in group 2, the older-sibling odds ratio was affected by day-care status. For those not in day care, the odds ratio for older siblings was significantly elevated; however, among those in day care the odds ratio was less than 1.

### Characteristics of Day-care Exposure Related to the Risk of Illness

Using exposure to a single day-care facility, we included 87%, 80%, and 72% of exposed children in age groups 1, 2, and 3, respectively, in the analysis. For each age group, the odds ratio of respiratory illness associated with current day-care exposure did not differ significantly between part-time (<40 hours/week) and full-time care.

For each age group the Figure displays how the duration of past day-care exposure influences the odds ratio of respiratory illness associated with current day-care exposure. Within each age group, the protective effect of longer enrollment in day care was statistically significant. In group 1 the odds ratio of respiratory illness for those exposed less than 9 months was 2.3 times as great as the odds ratio for those exposed greater than 9 months. Similarly, for those in age groups 2 and 3, exposure to day care for less than 9 months was associated with a 2.1- and 2.2-fold-greater odds ratio, respectively, than was exposure for 18 to 27 months. As

TABLE 3. Characteristics of Day-care Exposure\*

Characteristic	Age Group		
	6 wk-17 mo	18-35 mo	36-59 mo
Size of day-care facility			
2-6	133 (70)	167 (56)	141 (31)
7+	58 (30)	133 (44)	317 (69)
Prior time in day care			
<9 mo	116 (67)	94 (32)	154 (34)
9-18 mo	57 (33)	84 (29)	86 (19)
18-27 mo		88 (30)	88 (19)
>27 mo		27 (9)	128 (28)
Hours/wk in day care			
≥10-19	29 (15)	38 (13)	109 (24)
20-39	60 (32)	115 (38)	141 (31)
≥40	101 (53)	148 (49)	207 (45)

\* Results are given as number (%) of children.

**TABLE 4.** Illness and Events Within 2 Weeks Before Interview: Children Exposed (Exp) and Children Unexposed (Unexp) to Day Care, by Age Group\*

Illness/Event	Age Group					
	6 wk-17 mo		18-35 mo		36-59 mo	
	Exp	Unexp	Exp	Unexp	Exp	Unexp
<b>All Children</b>						
Respiratory illness	34.2	26.5	37.6	29.5	25.8	21.5
<b>Children With Respiratory Illness</b>						
≥2 symptoms	78.8	73.1	80.7	70.8	82.5	71.9
Symptoms for ≥2 days	98.3	100.0	95.2	92.6	96.4	92.9
Consulted/visited health care provider	66.1	60.4	49.5	43.4	55.3	39.1
Received antibiotics	40.7	31.1	29.9	25.0	35.0	19.8

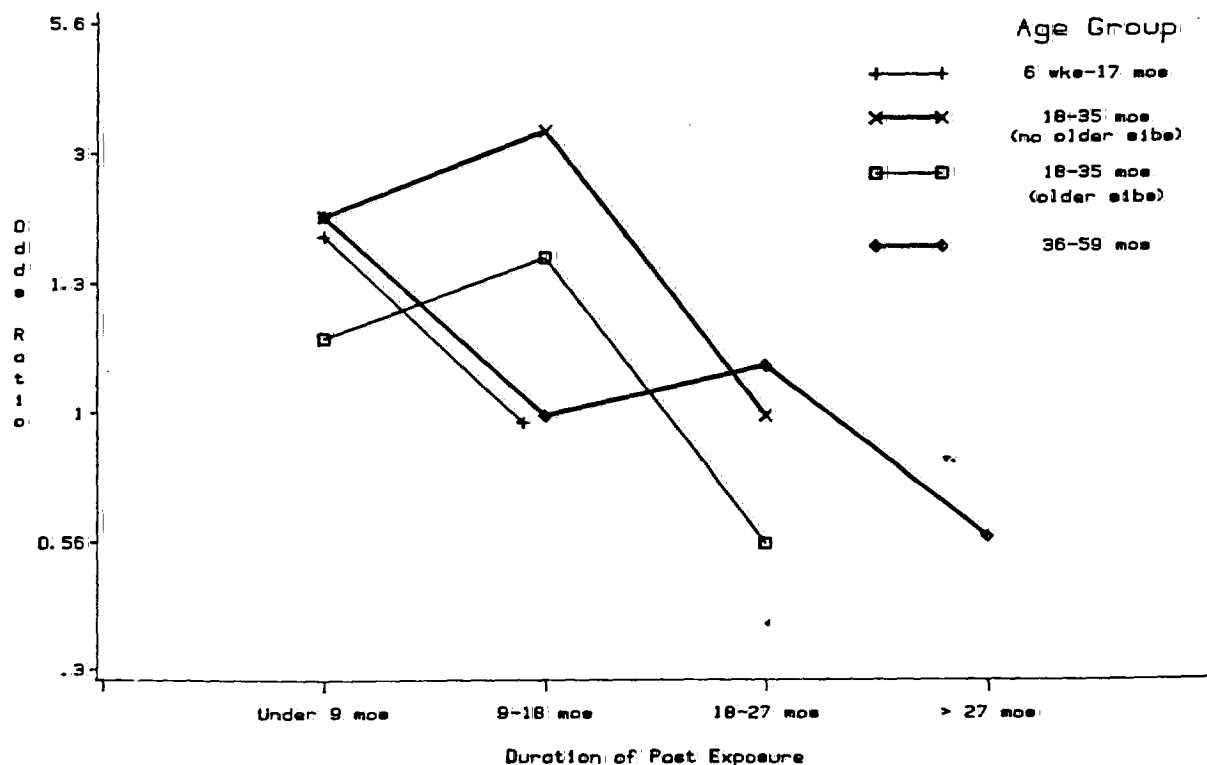
\* Results are percentages.

**TABLE 5.** Odds Ratios, by Age Group, for Respiratory Illness Associated With Day-care Exposure and With Having an Older Sibling\*

OR	Age Group		
	6 wk-17 mo	18-35 mo	36-59 mo
<b>Daycare OR (95% CI)</b>			
Older sibs		1.0 (0.65-1.6)	
No older sibs		3.4 (2.0-6.0)	
Aggregate†	1.6 (1.1-2.4)		1.3 (0.95-1.8)
<b>Older sibling OR (95% CI)</b>			
Day care		0.62 (0.38-1.0)	
No day care		2.1 (1.2-3.7)	
Aggregate†	1.7 (1.1-2.6)		0.60 (0.41-0.88)

\* OR, odds ratio; CI, confidence interval.

† Aggregate odds ratio used when no significant interaction observed.



**Figure.** Odds ratios of respiratory illness associated with day-care exposure by duration of past exposure and age group.

seen in the Figure, odds ratios well below 1 were observed in several situations. The odds ratio for children in group 3 who had been in day care for more than 27 months was 0.58 (95% CI, 0.23 to 1.1); the odds ratio for children in group 2 who had been in day care for more than 18 months and who had older siblings was 0.56 (95% CI, 0.22 to 1.03).

In each age group the odds ratio associated with larger (more than six children) vs smaller day-care facilities was elevated. This effect was greatest, and statistically significant, in group 2 (odds ratio = 2.2; 95% CI, 1.2 to 3.7). The odds ratios for large vs small centers were 1.6 and 1.4, respectively, for groups 1 and 3.

### Illness in Family Members

Respiratory illness in family members 5 years of age or older was highly correlated with the occurrence of respiratory illness in family members younger than 5 years of age in exposed and in unexposed families. Thirty-one percent (72/230) of exposed families with ill children younger than 5 years of age also reported a respiratory illness in a family 5 years of age or older compared with 12% (73/608) of exposed families with no ill children younger than 5 years of age; the comparable percentages for unexposed families were 36% (71/199) and 12% (90/744). Thirty-eight exposed families (4.5%), compared with 34 (3.6%) unexposed families, reported a respiratory illness in a family member 5 years of age or older that was preceded in the 2 weeks before interview by the onset of a respiratory illness in a family member younger than 5 years of age.

The results of the logistic model demonstrated that families that reported a respiratory illness in a member 5 years of age or older were 1.18 times as likely to have children in day care as were the families that reported no illness in a member 5 years of age or older (95% CI, 0.93 to 1.50).

### Attributable Risk

The ARE for respiratory illness was higher for groups 1 and 2 (28% and 33%) than for group 3 (18%). The PARs for the three age groups were 7.1%, 11.7%, and 7.7%, respectively. The similarity of the PARs in groups 1 and 3, despite the difference in AREs, reflects that a higher proportion of children in group 3 than in group 1 were exposed to day care.

### Infectious Illnesses in the Past Year

We compared the incidence rates of certain infectious illnesses in the year preceding the interview

by age and exposure status (Table 6). In each age group, the exposed incidence rate for chickenpox exceeded the unexposed rate; this difference was statistically significant for groups 1 and 3. No significant differences were observed in the incidence rates of selected other diseases listed in the table nor for respiratory-tract-related hospitalizations.

Because chicken pox was the only disease with enough cases for subset analyses, we used it to examine the effect of older siblings and the size of the day-care facility, two factors that are important for day-care-associated respiratory illness. Similar trends were observed. In groups 1 and 3 relative risks of more than 2 for day-care exposure were observed for the children with and children without older siblings. In group 2, however, only those without older siblings had an elevated relative risk (2.3); those with older siblings had a relative risk of 1.0. In addition, in each group, the risk for large centers exceeded that for small centers; relative risks of 1.6, 1.5, and 1.4 were observed for groups 1 through 3, respectively.

### DISCUSSION

The results of this nationwide study are consistent with observations from a number of studies conducted in smaller populations using a variety of methods, which suggest that day-care attendance is associated with an increased risk of respiratory illnesses in preschool-aged children.<sup>3-7</sup> In addition,

**TABLE 6.** Incidence Rates per 100 Child Years of Reported Infectious Illnesses in Past Year, by Age Group and Day-care Exposure\*

Disease	Age Group					
	6 wk-17 mo		18-35 mo		36-59 mo	
	Exp	Unexp	Exp	Unexp	Exp	Unexp
Chickenpox	9.5 <sup>  </sup>	3.5	11.2	8.2	19.5	8.3
Diarrhea lasting >1 wk	5.8	4.4	4.0	5.4	0.8	1.7
Vaccine-preventable diseases <sup>†</sup>	0.5	0.8	1.1	0.7	0.7	0.3
Other diseases <sup>‡</sup>	3.1	1.5	3.4	1.7	4.9	4.2
Respiratory-related hospitalizations <sup>§</sup>	3.0	3.1	2.1	2.0	0.3	0.0

\* Exp, children exposed to day care; Unexp, children unexposed to day care.

<sup>†</sup> Includes measles, mumps, rubella, diphtheria, and pertussis (no cases of mumps or diphtheria reported).

<sup>‡</sup> Includes mononucleosis, scarlet fever, scabies, lice, hepatitis, meningitis, giardiasis, and *Haemophilus influenzae* (no cases of hepatitis or meningitis reported).

<sup>§</sup> Includes pneumonia, influenza, bronchitis, asthma, and respiratory condition (unspecified).

<sup>||</sup> Significant difference between exposed and unexposed rate.

this study allowed examination of a number of issues, including the effect of prolonged exposure to day care and to older siblings, which had not been assessed in earlier studies. This study illustrates the complexity of this day-care-associated risk and the fact that a number of factors, including age of the child, presence of older siblings in the home, duration of prior day care, exposure, and size of the day-care facility may affect the risk of such illnesses.

The risk of respiratory illness associated with day-care attendance increased for children in all three age groups, although it was statistically significant only for (all) children in the youngest age group and children without older siblings in the 18-through 35-month age group. The highest risk was observed in this latter group (odds ratio = 3.4). The risk of respiratory illness in children aged 18 through 35 months with older siblings was not affected by day-care attendance; however, these children did have an excess risk of respiratory illness when compared with children who had neither older siblings nor day-care exposure. This group may have no day-care-related risk of respiratory illness because older siblings and day care pose similar and competing risks in this age group.

Although authors have speculated about differing day-care-related risks among children of different ages, earlier studies have not examined the risk of respiratory illness among children of different ages, and many have not included children older than 36 months of age.

Infants and toddlers in day care have also been shown to have increased risks of other illnesses, particularly diarrhea.<sup>6</sup> Inasmuch as many of the modes of transmission of agents commonly responsible for diarrheal and respiratory illnesses are believed to be similar—including child-to-child contact and fomites or shared objects, which are frequently mouthed by infants and toddlers—the increased risk of both types of illness is not unexpected. The higher day-care-associated rate of respiratory illness in children aged 18 through 35 months compared with younger and older children may be related to an increased frequency of such practices in this age group. Additionally, the lower day-care-associated risk (and absolute rates) of respiratory illness in children aged 36 through 59 months may be related to the acquisition of relative immunity to common respiratory agents. Although this study was not designed to assess all possible differences among children of different ages, it does illustrate the importance of considering age when examining day-care-related risk of respiratory illness.

Although there has been considerable speculation about the impact of early and long-term enrollment

in day care on the risk of various illnesses, especially respiratory illnesses, this is the first study to assess this factor using large cohorts of children who have been in day care for different lengths of time. Our results suggest that among children attending a single facility (87%, 80%, and 72% in age groups 1, 2, and 3, respectively), longer exposure was associated with a decreased risk of respiratory illness. This seemed to be true regardless of the size of the facility and was apparent in each age group. Among children aged 36 through 59 months, those who had been in day care for 27 or more months had a lower risk than those unexposed to day care (odds ratio = 0.5), suggesting that prolonged exposure to day care may lead to a reduced risk of respiratory illness among older preschool children. It is possible that this reduced risk of respiratory illness extends into the school-aged years and results in decreased absenteeism during this period. On the other hand, the increased rate of respiratory infections during the earlier years may be related to an increased risk of otitis media and associated complications, an issue our study did not address.<sup>9-11</sup>

This study suggests that the presence of older siblings in the home, as well as day-care attendance, has an important, and perhaps similar, impact on the risk of respiratory illness in children younger than 5 years of age. Among children aged 6 weeks through 17 months, the odds ratios associated with older siblings and with day care were similarly elevated. Among those 18 through 35 months of age, the odds ratio associated with older siblings among those not in day care was elevated but of smaller magnitude than the odds ratio for day care among those without older siblings. However, among children 36 through 59 months of age, the odds ratio associated with older siblings was less than 1 (odds ratio = 0.54,  $P < .05$ ), suggesting a protective effect. Thus, prolonged exposure to older siblings seemed to reduce the risk of respiratory illness.

Although risk of respiratory illness increased in association with day care, the size of the day-care facility significantly affected this risk only among those children 18 through 35 months of age; attendance at a larger facility (more than six children) was associated with a significantly increased risk of respiratory illness when compared with smaller facilities (two to six children, odds ratio = 2.2). Although there is considerable evidence that larger day-care facilities are associated with an increased risk of certain illnesses, including diarrhea and disease caused by *H influenzae*,<sup>6,12</sup> studies concerning the importance of the size of the facility have been less conclusive and have not attempted to evaluate this risk among children of different ages.

2023379840



Wald et al recently reported that children younger than 18 months of age in smaller day-care facilities (two to six children) had an intermediate risk of respiratory illness between home care and larger day-care facilities; in our study, however, the difference between small and larger settings was not statistically significant for children younger than 18 months of age.<sup>4</sup> Strangert, too, found no evidence that increasing the number of contacts to more than four to six children increased the risk of respiratory disease among children younger than 2 years of age.<sup>5</sup>

Although we observed no differences in the risk of a number of illnesses, including lower respiratory tract illness, meningitis, and measles, we had too few cases to adequately assess possible differences in the risk of these illnesses with respect to day-care attendance. However, the increased risk of chickenpox was statistically significant for those attending day care. Furthermore, chickenpox was similar to respiratory illness in terms of the influence of older siblings and the size of the day-care facility.

A major distinction of this study is that the participants represent a cross-section of day-care attendees and nonattendees in the United States. However, a number of limitations should be considered in assessing the results. The study primarily focused on illnesses occurring in the 2 weeks before the telephone interviews, which were conducted from March 17th through June 12th, rather than during the peak period of respiratory illnesses (winter months of December through March). Caution should be used in extrapolating these results to other seasons of the year.

Additional concerns include the possibility that the parents of children attending day-care centers may be more likely to report minor symptoms as illnesses because of a preconception that such facilities are associated with an increased risk of illness. However, most of the illnesses reported by parents involved two or more respiratory symptoms that lasted 2 or more days, and many involved antibiotic therapy; furthermore, these indices of severity were reported more frequently for exposed children than for unexposed children.

That this study consisted of a nationwide representative sample of children enrolled in day care makes the assessment of attributable risk potentially meaningful from a public health perspective. Our estimates that approximately 20% to 30% of respiratory illnesses among those attending day care can be attributed to day care and that 7% to 12% of all respiratory illnesses in children younger than 5 years of age occurring in the United States during the study period may have resulted from day-care attendance are similar to those reported

for children (all <36 months) in a study conducted in metropolitan Atlanta from mid-July to mid-September.<sup>3</sup> The present study also suggests that small, compared with larger, day-care settings, specifically for children 18 through 35 months of age, are associated with a reduced risk of respiratory illness. In addition, the study also illustrates that one possible result of early day-care enrollment may be a reduced risk of respiratory illnesses among older preschool children. Further studies, including studies prospectively observing large cohorts of children in various types of day-care settings, would help determine whether a reduced rate of respiratory illness extends into the school-aged years.

#### ACKNOWLEDGMENTS

We thank Larry Anderson, MD; Claire Broome, MD; Stephen Cochi, MD; Stephen Hadler, MD; Dennis Juranek, DVM; John Stewart, MD; and Robert Tauxe, MD, for their assistance in designing and supporting the study; the staff of Louis Harris and Associates, for collecting the data; and Vaughn Trader, for preparing the manuscript.

#### REFERENCES

- Henderson FW, Collier AM, Sanyal MA, et al. A longitudinal study of respiratory viruses and bacteria in the etiology of acute otitis media with effusion. *N Engl J Med*. 1982;306:1377-1383
- Denny FW, Collier AM, Henderson FW. Acute respiratory infections in day care. *Rev Infect Dis*. 1986;8:548-557
- Fleming DW, Cochi SL, Hightower AW, Broome CV. Childhood upper respiratory tract infections: to what degree is incidence affected by day-care attendance? *Pediatrics*. 1987;79:55-60
- Wald ER, Dahefsky B, Byers C, et al. Frequency and severity of infections in day care. *J Pediatr*. 1988;112:5400-5406
- Strangert K. Respiratory illness in preschool children with different forms of day care. *Pediatrics*. 1976;57:191-196
- Doyle A. Incidence of illness in early group and family day care. *Pediatrics*. 1976;59:607-612
- Bell DM, Gleiber DW, Mercer AA, et al. Illness associated with childcare: a study of incidence and cost. *Am J Public Health*. 1989;79:479-484
- Bartlett AV, Moore M, Gary GW, et al. Diarrheal disease among infants and toddlers in day care centers, II: comparison with day care homes and households. *J Pediatr*. 1986;107:503-509
- Pukander J, Sipila M, Karma P. Occurrence of and risk factors in acute otitis media. In: Lim DJ, Bluestone DC, Klein JO, et al, eds. *Recent Advances in Otitis Media With Effusion*. Philadelphia, PA: BC Decker; 1984:9-13
- Visscher W, Mandel JS, Batalden PB, et al. A case-control study exploring possible risk factors for childhood otitis media. In: Lim DJ, Bluestone DC, Klein JO, et al, eds. *Recent Advances in Otitis Media With Effusion*. Philadelphia, PA: BC Decker; 1984:13-15
- Ingvarsson L, Lundgren K, Olofsson B. Epidemiology of acute otitis media in children: a cohort study in an urban population. In: Lim DJ, Bluestone DC, Klein JO, et al, eds. *Recent Advances in Otitis Media With Effusion*. Philadelphia, PA: BC Decker; 1984:19-22
- Istre GR, Conner JS, Broome CV, et al. Risk factors for primary invasive *Haemophilus influenzae* disease: increased risk from day-care attendance and school age household members. *J Pediatr*. 1985;106:190-195

2023379841

**2023379842**